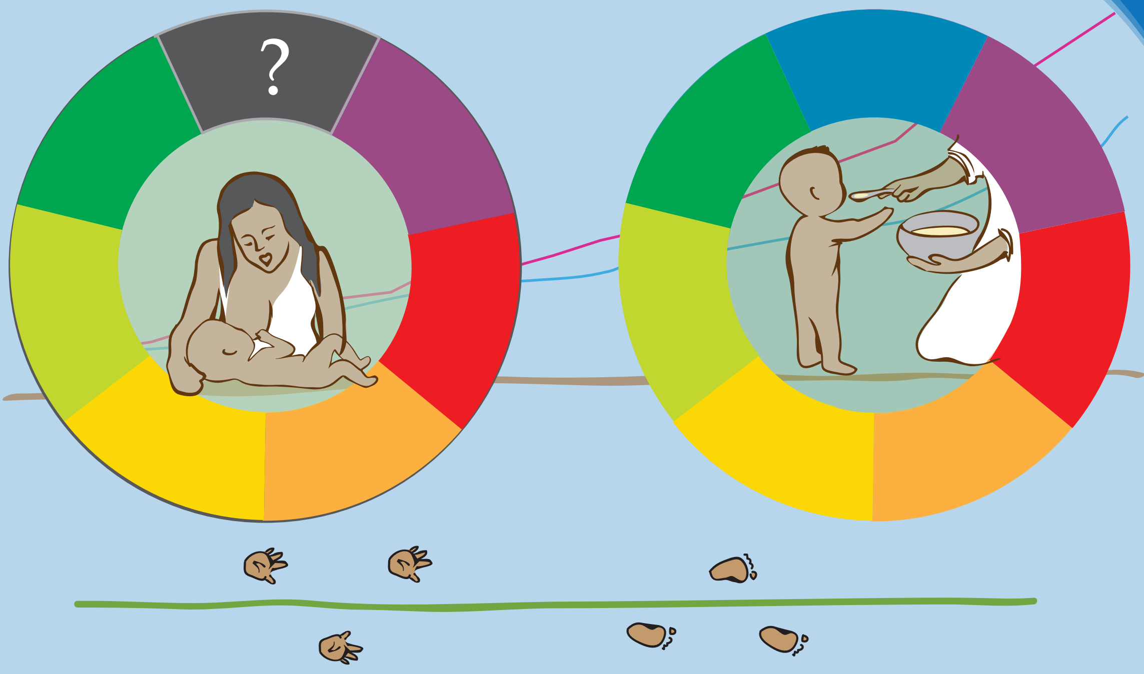
OPTIMIZING
YOUNG CHILD NUTRITION IN ETHIOPIA



The effectiveness, acceptance and possible risks of *micronutrient powders*

Aregash Samuel Hafebo

Propositions

1. Low iron dose micronutrient powders combined with integrated infant and young child feeding interventions are recommended for young children in Ethiopia to improve haemoglobin and linear growth.
   (this thesis)

2. Food-Based Dietary Recommendations based on locally available foods will improve the nutrient adequacy of diets of young children in Ethiopia.
   (this thesis)

3. One size fits all does not apply in research in general, and in program research in particular.

4. Diets of poor quality threaten health more than malaria, tuberculosis and measles combined. (Global Panel on Agriculture and Food Systems for Nutrition policy brief no. 12, November 2018)

5. More practice-based evidence is needed in order to have more evidence-based practice.

6. The essential difference between emotion and reason is that emotion leads to action while reason leads to conclusions. (quote from Donald Calne in Beamish G. et al., "Cave wall to internet, storytelling, the ancient learning art", Industrial and Commercial Training, 2015;47(4):190-194)

7. It is the possibility of having a dream come true that makes life interesting. (quote from Coelho, Paulo. “The Alchemist”. New York: HarperCollins, 1993).

Propositions belonging to the thesis, entitled

Optimizing Young Child Nutrition in Ethiopia: The effectiveness, acceptance and risks of Micronutrient Powders

Aregash Samuel Hafebo
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Optimizing Young Child Nutrition in Ethiopia

The effectiveness, acceptance and risks of Micronutrient Powders

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Optimizing Young Child Nutrition in Ethiopia

The effectiveness, acceptance and risks of Micronutrient Powders

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Thesis

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In loving memory of my father, Samuel Hafebo

Contents

Summary

Micronutrient deficiency in infants and young children has a negative impact on their health, growth, and development. Micronutrient malnutrition is one of the prevailing problems in developing countries. In Ethiopia, in spite of the country's progress in reduction of child malnutrition, these levels are still amongst the highest in the world, and little is known about the existence of gender differences in malnutrition and its causes. Ensuring optimal Infant and Young Child Feeding (IYCF) practices has been identified as one of the most effective public health interventions to improve child survival in developing countries. However, in Ethiopia local food-based dietary guidelines do not exist to provide guidance on how to ensure nutrient adequacy. Furthermore, the World Health Organization (WHO) recommends daily micronutrient powder (MNP) home-fortification for all young children in populations with a prevalence of childhood anaemia greater than 20% and when the diet does not include fortified foods. However, in Ethiopia concerns about the safety of iron-fortification interventions among iron-replete children have arisen because the daily provision of iron doses in home-fortification may exacerbate the presence and severity of infections in these children.

The overall aim of the study was to optimize complementary feeding practices to achieve nutrient adequacy and reduce anaemia without unacceptable health risks for young children in Ethiopia. This thesis is based on a cross-sectional study using secondary data from the 2011 national food consumption survey in four regions (Tigray, Amhara, Oromia and Southern Nations, Nationalities and Peoples (SNNP)) and an MNPs effectiveness study conducted in 35 *kebeles* (clusters) of 9 *woredas* (districts) of Oromia and SNNP, two of the large regions of Ethiopia.

In **chapter 2**, we performed a cross-sectional analysis using the baseline data of the MNPs effectiveness study conducted in March–April 2015. We examined the gender differences in determinants of nutritional status and the association of IYCF practices, dietary intake, mother and household characteristics with

stunting and wasting among infants aged 6-11 months (n=2036). We demonstrated that the prevalence of stunting and wasting varies among boys and girls (18.7% vs 10.7 % for stunting and 7.9% vs 5.4 % for wasting) respectively. Although poor IYCF practices were observed in both boys and girls, our analyses of predictors of stunting were not completely similar for each gender. Late initiation of breastfeeding (BF), non-exclusive BF, region of residence, and low maternal education are significant predictors of stunting in boys; untimely introduction to complementary foods (CF), low consumption of legumes/nuts were significant predictors of stunting in both sexes; and low consumption of eggs was a significant predictor of stunting only in girls. There was little indication for significant effect modification by gender. Only the association between stunting and initiation of breast feeding showed a large difference between boys and girls: it was a significant risk factor for stunting in boys (OR 1.46; 95%CI 1.02, 2.08), but clearly not in girls (OR 0.88; 95%CI 0.55,1.41). For wasting, region of residence and age of the mother are significant predictors irrespective of gender. Our finding supports the need for the development of gender-sensitive behaviour change intervention materials to convince mothers to timely introduce to BF and CF. More studies are required into the aetiology of stunting to provide evidence for policymakers envisioned for planning interventions.

Chapter 3 describes the analysis of data for 2504 children (6-23 months old) from the 2011 Ethiopian national food consumption survey. Results showed that dietary habits differ greatly across the different geographical regions in Ethiopia. Using linear programming, we formulated sets of region specific, and age-appropriate FBDRs to optimize nutrient adequacy for three different age groups (6-8, 9-11 and 12-23 months). Our results revealed that even if the developed FBDRs were fully adopted, intakes of zinc (in all age groups and regions), iron (for infants < 12 months of age in all regions), calcium, niacin thiamine, folate, vitamin B_{12}, and vitamin B_6 (in some regions and age-groups, but not in all) might remain suboptimal, indicating the need for additional interventions.

We used linear programming to determine whether (1) adding a locally produced CF consisting of grains and legumes, (2) adding MNPs, (3) adding a small quantity lipid-based nutrient supplements (Sq-LNS), (4) adding a combination of CF and MNPs or (5) of CF and Sq-LNS to the developed FBDRs could potentially improve the nutrient adequacy. The best option to achieve nutrient adequacy appeared to be a combination of regional FBDRs and home-fortification with daily MNPs for children 6-12 months of age and every other day for children 12-23 months of age. We also assessed the risk of inadequate and excess intake with these interventions using the estimated average requirement (EAR) cut-point method and full probability approach. It was confirmed that the proposed interventions would not lead to substantial excessive intake of iron and zinc. However, in addition to MNPs, alternative interventions also need to be explored to improve nutrient adequacy.

In **Chapter 4,** we assessed the effectiveness and potential risks of low iron dose (6 mg/serving) MNPs given every other day embedded in a local CF production programme in community based nutrition programme *woredas* (districts). We used a matched control quasi-experimental design. We assessed morbidity, growth and iron status of 6-23 months of age intervention and non-intervention children. A total of 2356 children, 1185 in the intervention group received MNPs (30 sachets/two months) for 8 months along with the CF from the Grain Bank programme, while 1171 in the non-intervention group who did not get both MNPs and CF, were included in the study. The caretakers in intervention areas were given instruction for the child to consume 15 sachets/month. The prevalence of anaemia showed a reduction (from 35.7 to 24.8%) in intervention children (but with no changes in the prevalence of iron deficiency) compared to a stable prevalence among non-intervention children (from 27.1 to 29.5%). Improved haemoglobin concentrations (with group-difference +3.17g/L), and improved linear growth with average increase in height (0.82cm; 95% CI 0.56-1.09, $p<0.001$) and weight (0.11kg; 95% CI 0.02-0.19, $p<0.011$) were observed in intervention compared to non-intervention children. Unexpectedly, serum ferritin (SF) did not change in the intervention group. This could have been due to the relatively low dose of iron provided, which might have been just sufficient to increase haemoglobin levels, but not enough to fill iron stores. In addition, intervention children were 2.31 times more likely to have diarrhoea and 2.08 times more likely to have common cold and flu than non-intervention children, but these differences decreased towards the end of the intervention. However, programs introducing MNPs should ensure adequate monitoring and management of morbidity.

In **chapter 5** using mixed (qualitative and quantitative) methods, we assessed factors associated with adherence and drivers for correct use of MNPs over time. Adherence to distribution (if mother gave the child $\geq$ 14 sachets MNPs per month) and adherence to instruction (if mother gave the child exactly 15($\pm$1) sachets MNPs per month) were assessed monthly by counting the used number of sachets. We observed an average of 58% for adherence to distribution and 28% for adherence to instruction, but adherence per month was found to fluctuate over time. Average MNPs consumption was 79% out of the total 120 sachets provided. Factors positively associated with adherence included: ease of use, child liking MNPs, support from community and mother's age >25 years. Distance to the health post, knowledge of correct use, perceived negative effects and living in SNNP region were inversely associated with adherence. MNPs are promising to be scaled-up, by taking into account factors that positively and negatively determine adherence. For instance, community factors to increase adherence could include focusing on strengthening social support such as empowering husbands and health workers to be more involved in the programme.

Finally, **Chapter 6** summarizes the main findings; and reflects on the internal and external validity of the studies addressed in this thesis. The strengths of the study related to the embeddedness in a "real-life" setting with frequently repeated measurements of data collection, are discussed. Furthermore, possible limitations of the studies related to the non-randomized quasi-experimental design of the effectiveness study, the limited control on the functionality of the Grain Bank programme, reliance on memory of respondents on dietary intake, morbidity and MNPs intake; and measures taken to reduce effect on study results are also reflected.

In conclusion, we confirmed that stunting and wasting levels are high in Ethiopia, especially among boys, with timely introduction to breastfeeding having more impact on growth of boys, and timely introduction of complementary foods impacting growth of both boys and girls. Adopting region-specific food based dietary guidelines developed for children 6-23 months old showed to have potential to improve nutrient intake but need to be combined with alternative strategies to reach nutrient adequacy. The applicability of the developed FBDRs needs to be tested among children 6-23months of age in the study regions. We also showed that MNPs with low iron dose are acceptable combined with other IYCF interventions, and improved haemoglobin status and linear growth in 6-23 month old children with only mild side effects. Nevertheless, programmes introducing MNPs in the context of an integrated infant and young child nutrition intervention should ensure adequate management, monitoring and control of diarrhoea.

Chapter 1

General introduction

Malnutrition, meaning any imbalance in satisfying nutrition requirements, is a problem of public health concern in most developing countries[1], including Ethiopia. Young children's rapid growth and inadequate dietary practices, especially in poor countries, make them vulnerable to nutritional deficiencies. Many children suffer from undernutrition and growth faltering during the first 1000 days of life, with consequences that persist throughout their life. Stunting and anaemia are the most prevalent forms of undernutrition in developing countries[3].

Stunting levels, defined as height-for-age z-scores below -2 standard deviations, are reducing globally (from 32.6% in 2000 to 22.2% in 2017)[4]; however, the reduction is slowing down especially in Sub-Saharan African (SSA) countries (from 45.7% in 2000 to 35.6% in 2017)[4]. Stunting is the result of poor nutrition in-utero and during early childhood[4]. Epidemiological studies show that stunting is also frequently associated with repeated exposure to poor sanitation and hygiene and individual factors like a child's gender and poor economic conditions[5,6]. Most notably, child morbidity[6-8] and inadequate infant and young child feeding (IYCF) practices[9,10] have been identified as immediate causes of child stunting, and reciprocally morbidity due to diarrhoea and pneumonia is one of the major consequences of child undernutrition, making the condition even worse. The WHO/CHERG[1] 2014 estimates that diarrhoea contributes to more than one in every ten (13%) child deaths in Ethiopia[11].

Anaemia is defined as haemoglobin concentration below 110g/L (in children 6–59 months of age) and characterized by a low number of red blood cells in the body[12]. Anaemia is a major public health problem affecting a large number (30%) of the population globally[13]. Among children under the age of 5 years, the highest anaemia prevalence (55%) of any region is in East Africa[14].

[1]Child Health Epidemiology Reference Group

African children, particularly those aged 6–23 months, have the highest prevalence, 64.7%; this represents one-third of the global burden of anaemia[15]. Anaemia affects cognitive and motor development adversely and causes fatigue[16]. The causes of nutritional anaemia are multifaceted, including nutrient deficiencies (of iron, Vitamin B_{12}, and folate)[3], high physiological demands in early childhood, and iron losses from parasitic infections[17].

The consequences of stunting and anaemia affect not only the individual's optimal growth and mental development[18,19], but also national economic development, resulting in productivity losses and perpetuating poverty[20] in the population. Hence, major efforts are needed to rapidly and sustainably improve the nutritional status of infants and young children. Ensuring optimal IYCF practices, including optimal complementary feeding practices, has been identified as one of the most effective public health interventions to improve child survival, growth, and development in developing countries[21-25].

Importance of infant and young child feeding practices

The first 1000 days, the period during pregnancy and a child's first two years of life, are considered a critical window of opportunity for prevention of growth faltering[26]. Adequate intake of (micro)nutrients through appropriate IYCF is critical during this period for child growth and mental development[27]. According to the global IYCF strategy, the focus should be on the importance of investing in protecting, promoting, and supporting appropriate IYCF practices[28]. This is to ensure that children develop to their full potential, free from the adverse consequences of compromised nutritional status and preventable illnesses[28]. The strategy further emphasizes the use of suitable locally available foods while introducing complementary foods[29].

The core components of appropriate IYCF practices are early initiation of breastfeeding, exclusive breastfeeding (EBF), continued breastfeeding at 1 year, timely introduction to complementary foods, minimum dietary diversity, minimum meal frequency, minimum acceptable diet, and consumption of iron-rich or iron-fortified foods[2], see Box 1. Early initiation of breastfeeding offers an important advantage in protecting the child from mortality and severe morbidity[30,31]. Colostrum – a fluid produced by the mother immediately after giving birth – is a rich source of nutrients, antibodies, and growth factors for the infant[32]. EBF improves health status, promotes the growth of new-borns[28], and reduces the prevalence of children suffering from gastrointestinal and respiratory infections[33,34]. It is also recommended by WHO as the most effective way of reducing childhood morbidity[35] and known for preventing early childhood deaths[36]. EBF has beneficial effects also on children's cognitive development[37].

An appropriate transition from exclusive breastfeeding to complementary feeding is required at the age of 6–8 months because the second half of an infant's first year is an especially vulnerable time, when breastmilk alone is no longer sufficient to meet his or her nutritional requirements. A too early or a delayed introduction to complementary foods leads to poor nutritional status and increased morbidity[24,38,39]. Iron and zinc are reported to be the most problematic nutrients during this period[40,41]. Studies report that the amount of food that can be consumed apart from breastmilk is relatively small. The child therefore needs to have frequent meals, with frequency depending on age and high nutrient-dense complementary foods[40].

Diversified semi-solid and solid foods as complementary foods are required to ensure adequate intake of nutrients and support rapid growth and development. Failure to achieve minimum dietary diversity is negatively associated with stunting[42]. In most

Box 1. Core infant and young child feeding practices

- **Early initiation of breastfeeding:** provision of mother's breastmilk to infants within one hour of birth
- **Exclusive breastfeeding:** means that an infant receives only breastmilk from his or her mother or a wet nurse, or expressed breastmilk, and no other liquids or solids – not even water – with the exception of oral rehydration solutions, or drops/syrups of vitamins, minerals, or medicines, until 6 months
- **Continued breastfeeding at 1 year**
- **Timely introduction of solid, semi-solid, or soft foods (6–8 months)**
- **Minimum dietary diversity:** consumption of four or more food groups from the seven food groups, namely: grains, roots, tubers; legumes and nuts; dairy products (milk, yogurt, cheese); flesh foods (meat, fish, poultry, liver/organ meats); eggs; vitamin A-rich fruits and vegetables; other fruits and vegetables
- **Minimum meal frequency:** consumption of 2 or more (at age 6–8 months), 3 or more (at age 9–23 months) solid or semi-solid feeds for breastfeeding children, or 4 or more solid or semi-solid or milk feeds for non-breastfeeding children at age 6–23 months
- **Minimum acceptable diet:** a combination of minimum dietary diversity and minimum meal frequency
- **Consumption of iron-rich or iron-fortified foods.**

Source: WHO. Indicators for assessing infant and young child feeding practices. Part 1 definitions[2]

developing countries, the traditional complementary foods are typically prepared from cereals and usually contain low amounts of bioavailable micronutrients such as vitamin A, iron, and zinc, but rather have high amounts of phytate, which interferes with the absorption of iron and zinc[43]. Suboptimal IYCF practices include the dilution of traditional complementary foods with water[44] and the use of, for instance, contaminated water, a potential route for diarrhoea transmission among infants[45]. Adequate iron and zinc intakes are reported to be difficult during this age[40,41]. The inclusion of animal-source foods is required to meet the need for such micronutrients. However, in many populations, this might not be feasible, especially in developing countries. Consequently, in most cases, nutrient supplements or fortified food are required to meet nutrient adequacy[46,47]. In addition, limited access to a safe water supply, inappropriate sanitation systems, and unhygienic conditions in and around homes all influence the spread of infectious diseases.

This thesis describes studies that contribute to a better understanding of how to improve the feeding practices and nutritional status of young children in Ethiopia. This chapter introduces the studies by describing the nutrition situation and IYCF practices in Ethiopia, followed by a description of policies, programmes, and challenges for improving IYCF, and the possible interventions to improve nutritional status. It highlights the main objectives addressed and closes with a short outline of the thesis.

Nutritional situation in Ethiopia

Undernutrition in Ethiopia

As in other SSA countries, the rate of change in undernutrition in Ethiopia is slow. The 2016 Ethiopian Demographic and Health Survey (DHS) shows that between 2000 and 2016 stunting reduced from 58% to 38%, underweight dropped from 41% to 24%, and wasting decreased from 12% to 10% (Figure 1). Despite this progress in reducing child malnutrition, these levels are still amongst the highest in the world. Child undernutrition also comes at a high economic cost, estimated in Ethiopia to amount to USD 4.7 billion per year or 16.5% of GDP[48].

Apart from protein-energy malnutrition, micronutrient deficiencies, particularly in iron, iodine, and vitamin A, are considered important public health problems in Ethiopia[49]. They contribute significantly to morbidity and mortality among children[50]. According to the 2016 Ethiopian DHS, the overall prevalence of anaemia among children aged 6–59 months was 57%[11] and 34.4% according to a national study carried out by the Ethiopian Public Health Institute (EPHI) in the same year[51], indicating a severe public health problem[52]. However, there are large regional variations, for example with high prevalence in the Oromia (66%) and South Nations, Nationalities, and Peoples (SNNP) (50%) regions[11]. Prevalence of iron deficiency (as measured by serum ferritin) in preschool children was 17.8% in 2015[51], but no national data are available for preceding years. The national prevalence of goitre among 6–12 year olds was 39.9% by 2005[53], increasing to 48% in more recent studies[51]. National data on the prevalence of iodine deficiency in young children are not available. The national prevalence of subclinical vitamin A deficiency in 2006 was 37.7%[54]; this reduced to 14% in 2015[51].

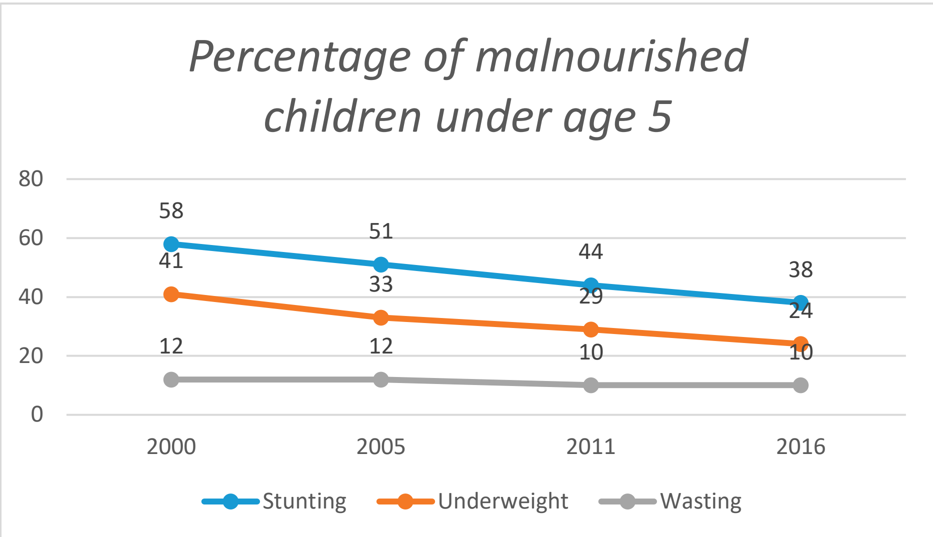

Figure 1. Trends in nutritional status of children in Ethiopia

Source: CSA. Ethiopia demographic and health survey 2016[11].

Infant and young child feeding practices in Ethiopia

According to the 2016 Ethiopian DHS, 73% of children began breastfeeding within one hour of birth, 58% of children were exclusively breastfed, and 60% of children were introduced to complementary feeding at 6–8 months. The report also shows a small improvement in IYCF practices since 2011; for instance, in the minimum dietary diversity (from 4.8% to 14%) and in the minimum acceptable diet standards (from 4% to 7%). However, the proportion of children with a minimum meal frequency has displayed a decreasing trend from 48.5% to 45% since 2011[11,55].

Several factors are reported to affect IYCF practices in Ethiopia. For instance, timely initiation of breastfeeding could be affected by societal beliefs favouring starting with pre-lacteals (other feeding), lack of adequate support in health facilities and in the community, aggressive promotion of infant formula through media, and lack of knowledge, encouragement, and advice by family and friends[31]. Furthermore, children's dietary diversity is extremely low, and foods from animal sources are rarely served to children[56-58]. Optimum childcare practices are also influenced by maternal education and the wealth of the child's family[59-61]. Although Ethiopia has a wide range of agro-climatic conditions and grows a variety of cereals, root crops, and vegetables, some of these are not fully utilized. Often, regions depend on a single food crop – cereals and root crops such as *enset* and maize in the south and southwest of the country[62]. Moreover, it is not common to use fortified complementary feeding, especially in rural areas[63,64].

With regard to gender differences in nutritional status, recent studies have reported that boys tend to have a higher prevalence of stunting than girls in SSA[65,66]. Several studies have demonstrated that gender differences in nutritional status during infancy are explained by the differences in early introduction of complementary feeding to boys compared to girls, for instance in

Senegal[65], thereby reducing the period of exclusive breastfeeding for boys. It is not known whether these gender differences also exist in Ethiopia.

Policy environment, strategies, and programmes to address nutrition-related public health problems in Ethiopia

The National Nutrition Strategy (NNS) of Ethiopia was endorsed in February 2008 to address nutrition-related problems and interventions in the country[50,67]. The importance of averting growth faltering at an early age by providing basic nutrition intervention programmes such as promoting essential nutrition actions[68], child growth monitoring and promotion services[69], and micronutrient supplementation and fortification[70] were emphasized, including mechanisms for the control and prevention of micronutrient deficiencies[67]. According to the NNS, nutrition policy needs to be implemented at all levels of multiple sectors simultaneously, such as health, agriculture, and education, to realize the expected outcome.

The NNS was implemented through National Nutrition Programme (NNP) I (2008–2013)[58]. NNP I was revised in 2014 with important principles and strategies addressing, for instance, nutrition problems through multisectoral linkages, focusing on the life-cycle approach to accelerate stunting reduction, and aligning the NNP objectives with the second national strategic framework for economic development: the country's Growth and Transformation Plan (GTP, 2015/16–2019/20)[49]. NNP II was launched in 2016, focusing on the first 1000 days of life to eradicate chronic malnutrition by 2030[71]. NNP II comprises several initiatives and programmes, including promoting, supporting, and creating access to appropriate complementary feeding for 6–23-month-old children. Performance indicators and targets were identified for each initiative. For instance, the 2020 targets of NNP II include reducing the prevalence of stunting among under-5 children from 40% to 26% and increasing the proportion of children 6–23 months with a minimum dietary diversity score from 5% to 40%[71]. The Community-Based Nutrition (CBN) programme – a key component of NNP – comprises the implementation of a comprehensive and integrated nutrition services package[72] to strengthen service delivery at facility and community level. This package is an approach that links all nutrition programmes (such as CBN, community-based management of acute malnutrition, enhanced outreach strategy/child health days, and maternal, adolescent, infant, and young child nutrition)[72] that aim to reduce malnutrition through various nutrition services such as screening, case management, supplementation, deworming, and counselling at community level[58].

Several small-scale and shorter-term infant and young child nutrition programmes have been implemented in Ethiopia under NNP I and II[38,73]. These programmes have shown that it is feasible to improve IYCF practices, food diversity, and food quantity with comprehensive approaches that combine capacity building and behaviour change interventions to improve food availability, e.g. with home gardening[38,73,74]. In line with NNP I, the Government of Ethiopia together with partners started to implement the CBN interventions in 2008 to improve IYCF practices in the four agrarian regions of the country (see Figure 2). In this context, UNICEF Ethiopia, together with the Food and Agriculture Organization (FAO) of the United Nations and local universities, implemented a pilot project involving two general models (rural and semi-urban) for community-based complementary food production through a grain bank system (further referred to as Grain Bank programme). This pilot focused on increasing the availability, demand, and nutritional adequacy of the complementary foods by piloting a bartering system in rural areas and central production by women's groups in semi-urban areas. The focus was on an improved grain/legume blend as the base for complementary foods. The objective of the programme was to increase the number of infants and young children with sustained consumption of complementary food adequate in macro- and micronutrient content to improve their growth. Later, this pilot was extended and rolled out in some of the CBN *woredas* (districts) through collaboration with the international NGO, Nutrition International[75].

Although the Grain Bank programme has brought several additional benefits to the community, some challenges were identified in relation to the need to have a strong management structure to guide its implementation, the feasibility of integration with existing health structures, and the sustainability of supply during food shortages[76]. The feasibility of implementing the rural model grain bank depends on the continuous supply of raw materials and labour. The labour expenditure for production and processing of complementary food depends on a group of volunteer women from the respective *kebeles* (clusters), and this is unlikely to be sustainable without fair compensation or incentives. External inputs such as sugar, milling, and transportation costs were covered by partners, reducing the likelihood of continuation of such a programme when external support withdraws. One of the major challenges identified was the absence of government-endorsed food-based dietary recommendations (FBDRs) to guide the formulation of appropriate complementary feeding of young children in Ethiopia. Second, the low nutrient density of the local complementary foods from the grain banks created a need for supplementation with other sources of micronutrients through further dietary modification and fortification to practically improve child nutrition[75]. Third, little is known about the existence of gender differences in nutritional status and underlying IYCF practices in Ethiopian infants, which, when present, should be addressed in behaviour change communication alongside the Grain Bank programme. In the next section, the knowledge gaps that hamper progress towards addressing these challenges is further described.

Knowledge gaps

Food-based dietary recommendations

Evidence-based and suitable FBDRs are essential to guide the identification and provision of appropriate complementary foods for young children. In Ethiopia, there are no government-endorsed evidence-based FBDRs that could inform IYCF guidance in, for example, the CBN activities relating to promoting, educating, and advising mothers on optimum IYCF practices.

Linear programming (LP) is a mathematical method that can be used to develop complementary food guidelines based on the habitual dietary intake of the population. Optifood is a software program developed by WHO in collaboration with the London School of Hygiene and Tropical Medicine, Food, and Nutrition Technical Assistance III Project (FANTA) and Blue-Infinity to design population-specific FBDRs using LP approach. LP tools such as Optifood are found to be advantageous compared with conventional, expert-based approaches because of the objectivity and strength of evidence used to develop the recommendations. This mathematical modelling approach has been used successfully in analysis such as designing optimal food-based recommendations for young children and adults[77-79], studying the impact of cost constraints on food choices[80], assessing the economic value of introducing fortified foods and food aid[81-83], and assessing the effect on nutrient adequacy of introducing (biofortified) foods or supplements[84,85]. This method offers the advantage of being an objective approach based on local foods and current dietary patterns, and therefore the food-based guidelines are likely to be adhered to[77,86].

Optifood can be used to study whether food-based dietary guidelines based on locally available foods can be formulated to address the nutrient adequacy of infants and young children, and whether additional interventions are needed to reach nutrient adequacy. It can also test various supplementation scenarios to see which option would give the best nutritional profile. In addition, the risk of inadequate and excess nutrient intake needs to be checked against the estimated average requirement to assess the extent to which the modelling improves the nutritional intake and also whether the nutritional intake exceeds the tolerable upper level[87-89].

Home fortification with micronutrient powders

Home fortificants like micronutrient powders (MNPs) and small-quantity lipid-based nutrient supplements (Sq-LNS) including iron are available for interventions. MNPs (sometimes also referred to as sprinkles) are powdered, single-dose packets (1g each) containing multiple vitamins and minerals in powder form that can be sprinkled into any semi-solid food[90]. "Sprinkles" is the trademarked name for one particular brand of MNPs[91]. MNPs in general contain 12.5mg iron as encapsulated ferrous fumarate together with 14 other vitamins and minerals[1] [92]. WHO recommends the use of iron-containing (12.5mg) MNPs for home fortification to improve iron status and reduce anaemia among children aged 6–23 months[92]. Sq-LNSs[2] or fat-based supplements provide energy, protein, and essential fatty acids in addition to minerals and vitamins to address macro- as well as micronutrient deficiencies and enhance the absorption of fat-soluble vitamins[93,94]. Sq-LNSs (20g dose) are designed to prevent undernutrition and promote the growth and development of infants and young children. The 20g dose is designed to avoid displacement

[1]WHO-recommended (6–23 months children) composition of MNP per sachet: iron 10 to 12.5mg (elemental iron), vitamin A 300µg of retinol, zinc 5mg, vitamin C 30mg, thiamine 0.5mg, riboflavin 0.5mg, niacin 6mg, vitamin B_6 0.5mg, folate 150µg dietary equivalents, vitamin B_{12} 0.9mg, vitamin D 5µg, vitamin E 5 TE, copper 0.56mg, selenium 17µg, iodine 90µg

[2]Composition of Sq-LNS (Nutributter) per 20g packet: energy 118 kcal, protein 2.6g, water 4g, fat 9.6g, carbohydrate 5.3g, calcium 280mg, iron 6mg, zinc 8mg, vitamin C 30mg, thiamine 0.3mg, riboflavin 0.4mg, niacin 4mg, vitamin B_6 0.3mg, folate 80µg dietary equivalents, vitamin B_{12} 0.5mg, vitamin A 300µg of retinol

of breastmilk and allow for dietary diversity. Unlike MNPs, Sq-LNSs may also be eaten as is (directly from the packet)[93].

Pros and cons of an intervention with MNPs

The benefits of improved micronutrient intake are well documented[95]. Home fortification of complementary foods with MNPs has several advantages: it does not require major changes in dietary practices, allows the child to get a full dose of the required micronutrients by mixing it in a small quantity of food, is better accepted than medicinal iron drops and less expensive than fortified complementary foods[95]. In addition, the iron absorption of supplements is better than that of fortified foods[96]. Combined supplementation (iron and vitamin A) has been found to be more effective than single supplementation[97]. The advantage of MNPs over other supplements is their fast and flexible preparation. Several studies report the benefits of MNPs; for instance, haemoglobin concentrations increased and iron status improved in Vietnamese 6–24-month-old children[43] and 1–3-year-old Indian children[98]. Efficacy studies in 14 countries demonstrate significant positive effects on growth within the first year of life[99]. Studies also suggest that the provision of iron to children with iron-deficiency anaemia can enhance motor and cognitive development (together with reducing the prevalence of severe anaemia)[95,100]. A study in Ghana reports that MNPs were well accepted and resulted in significantly improved iron status in the intervention group compared with the control group[95].

However, side-effects of MNPs have also been reported, and concerns have arisen around the safety of iron-supplement interventions among iron-replete children, because the daily provision of supplemental doses of iron may exacerbate the presence and severity of infections, including malaria and diarrhoea[101,102]. Iron is an essential micronutrient for infant growth[100], but it is also an essential nutrient for many pathogenic bacteria in the gut[103]. Excess iron intake (by fortification or supplementation) promotes the growth of these pathogenic strains and might modify the balance of microbial species[103]. Reported potential side-effects of MNPs include increased morbidity, for instance diarrhoea and acute respiratory infections[101,102]. In Ethiopia, the prevalence of anaemia in children 6–59 months of age is high[11], but the National Food Consumption Survey (NFCS)[104] reported also high iron intakes in children 1–3 years of age in Ethiopia. This raises questions regarding whether additional interventions with iron are necessary and safe, necessitating a thorough assessment of the benefits and potential risks of MNPs. Usually, a lower dose of iron in MNPs is preferred in a community setting because of the anticipated fewer side-effects. There is also some evidence suggesting that zinc absorption may be negatively affected by higher doses of iron[105]. However, the efficacy of low-dose-iron interventions and their side-effects should be determined to address the concerns of the implementing bodies, including the government.

Adherence to intervention

Studies on the acceptability of MNPs have found that acceptability and compliance are generally high among caretakers and mothers[90,95]. One of the factors affecting adherence is ease of use, as reported in a study in Ghana, where only 16% of mothers experienced negative effects and problems with using sprinkles[95]. Three studies reported that children's appetite increased compared with the pre-intervention period and that sprinkles did not affect the colour or taste of the food[106-108]. High acceptability and correct preparation of the sprinkles among mothers were reported in Kenya[109]. Potential barriers were also identified, and various factors, including knowledge, experience with sprinkles, availability, costs and individual characteristics, families and social networks, local cultures, the behaviour of health workers, or the intervention design, may influence adherence[110]. Additionally, several studies have revealed that mothers prefer a less structured dosing regimen than a rigid one[111,112]. For example, flexible administration of MNPs led to higher adherence rates in a Bangladesh study[111]. Maintaining adherence over a long period of an MNP intervention is challenging, because anticipation and motivation among beneficiaries are likely to decline over time[111]. It is relevant to investigate whether adherence varies or improves through time. As poor adherence is a modifiable behaviour and can potentially be improved[113], but is context specific, it is important to get context-specific insights about caregivers' perceptions of MNPs and the influence of social support, through, for instance, empowered husbands and health workers[114,115] to inform future directions for policymakers.

Rationale

Poor complementary feeding practice is the single most important contributor to the high rates of childhood undernutrition observed in many developing countries, including Ethiopia. To alleviate this problem and to improve the macro- and micronutrient density of the complementary foods for children, evidence-based, realistic, and suitable FBDRs are essential. These will also demonstrate how locally produced complementary foods can fit into these recommendations, in addition to other foods consumed, and also what additional interventions might be required to further improve diet quality. An additional intervention is the use of MNPs; however, given the existing concern in Ethiopia about the safety of high-iron-dose MNPs, the effectiveness as well as potential risks of low-dose-iron MNPs need to be investigated. Furthermore, the feeding recommendations resulting from this study can be used in IYCF counselling to mothers/caregivers; evidence on the effectiveness and safety of MNPs will add to the necessary information needed for the development of policies concerning the need for additional supplementation of younger children in the form of MNPs.

Aim and objective

The overall aim of the study is to optimize complementary feeding practices for young children in Ethiopia. The specific objectives are:

- To explore gender differences in nutritional status and IYCF practices in children from two regions in Ethiopia;
- To develop optimized (local) food-based complementary feeding recommendations in four regions in Ethiopia;
- To evaluate the effectiveness of an integrated package of interventions – including distribution of locally produced complementary foods through the Grain Bank programme and low-iron-dose MNPs – on growth, iron and haemoglobin status, and morbidity of infants and young children;
- To investigate the determinants of adherence to the use of MNPs over time.

Outline of the thesis

This thesis is based on secondary data analysis of the NFCS of four agrarian regions in Ethiopia and an MNPs effectiveness study in two regions in Ethiopia. **Chapter 2** describes the gender differences in the prevalence of nutritional status, the association of stunting and wasting with IYCF practices, and their determinants among 6–11-month-old infants living in selected *kebeles* (the smallest administrative unit in Ethiopia) in the Oromia and SNNP regions. This chapter is based on baseline data collected in March–April 2015 for the MNPs effectiveness study. In the NFCS, nationally and regionally representative individual dietary intake data for young children were available for four large agrarian regions, namely Amhara, Tigray, Oromia, and SNNP; these were collected in June–September 2011. In **Chapter 3**, using LP (Optifood), we used the NFCS data to formulate FBDRs and test the ability of additional nutrition interventions (MNPs and Sq-LNSs) to improve the nutrient adequacy of diets of 6–23-month-old children. In **Chapter 4**, the effect of low-iron-dose MNPs on the iron status, growth, and morbidity of young children is presented and compared with a matched control group using a quasi-experimental design. **Chapter 5** explores the use, and determinants of adherence to the use, of MNPs through a knowledge, attitude, and practice study. We additionally conducted in-depth interviews and focus group discussions in order to obtain further information about factors positively or negatively affecting adherence to the use of MNPs. Finally, in **Chapter 6**, the main findings are summarized, methodological considerations and practical implications are discussed, and conclusions and recommendations for future research are presented.

Study setting and site selection

The studies described in this thesis were implemented in the framework of the Grain Bank programme, adding a component of home fortification with MNPs. The implementing partners were UNICEF, Nutrition International (NI), EPHI, and Wageningen University. This programme also provided an opportunity for EPHI and NI, together with Wageningen University, to incorporate rigorous programme monitoring in order to assess the risks and benefits of providing iron along with other micronutrients to young children living in low-income country settings.

The quasi-experimental longitudinal study was implemented in two regions in Ethiopia: Oromia and SNNP. Both regions were selected because of their proximity to the capital (for transportation of samples, see also Figure 2) and because they are representative of a large part of the Ethiopian population[116]. Moreover, these regions were selected because of their high level of food insecurity, poor infant feeding practices, and poor child nutritional status as assessed by the 2016 Ethiopian DHS[11]; these characteristics are representative of the situation in Ethiopian villages. Subsistence farming is a typical feature of agriculture in Ethiopia, and the study areas are basically rural agrarian communities. In Oromia and SNNP, 77% and 73% of households, respectively, rely on crop production, livestock, or a combination of the two[117]. Given this high dependence on farming and a high reliance on home-produced food, rainfall is one of the major determinants of food security[117]. *Woredas* (districts) implementing CBN activities were selected because they had suitable existing infrastructures and programmes like child health days and growth monitoring and promotion programmes to support our intervention.

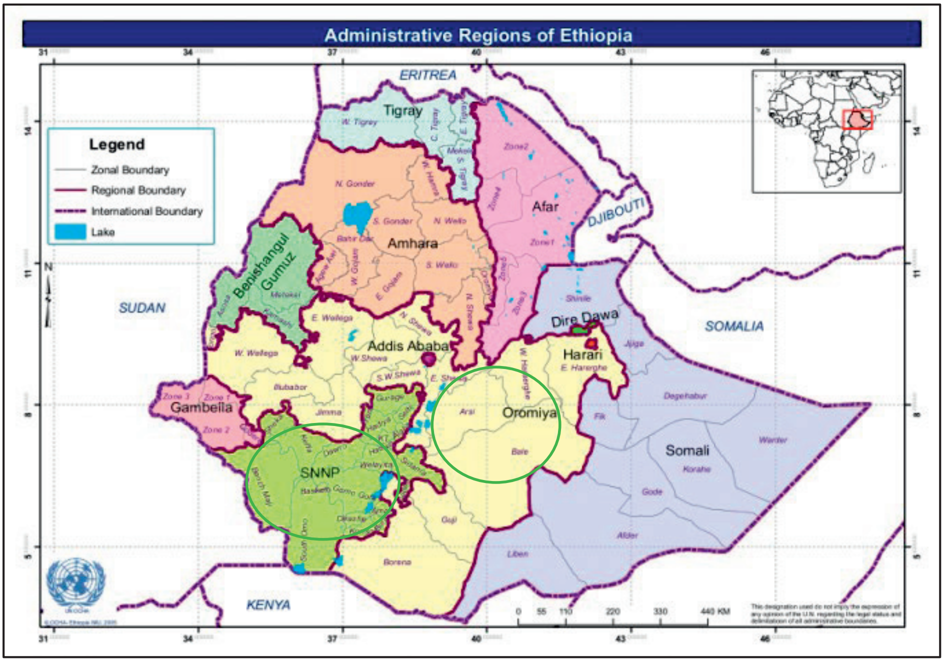

Figure 2: Map of study area

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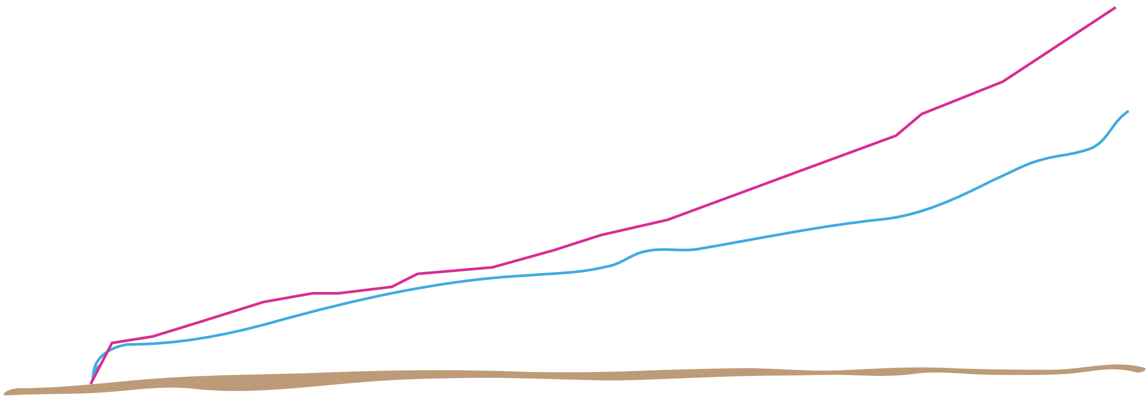

Chapter 2

Gender differences in nutritional status and determinants among infants (6–11m) in Ethiopia

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Abstract

Background: A limited number of studies suggest that boys may have a higher risk of stunting than girls in low-income countries. Little is known about the causes of these gender differences.

Objective: To assess gender differences in nutritional status and its determinants among infants in Ethiopia.

Methods: We analysed data for 2036 children (6–11 months old) collected as the baseline for a multiple micronutrient powders effectiveness study in two regions of Ethiopia in March–April 2015. Child, mother, and household characteristics were investigated as determinants of stunting and wasting. Multiple logistic regression models were used separately for boys and girls to check for gender differences while adjusting for confounders.

Results: Stunting and wasting prevalence is significantly higher among boys compared to girls, 18.7 vs 10.7% and 7.9 vs 5.4%, respectively. Untimely initiation of breastfeeding, non-exclusive breastfeeding, region of residence, and low maternal education are significant predictors of stunting in boys. Untimely introduction to complementary food and low consumption of legumes/nuts are significant predictors of stunting in both boys and girls, and low egg consumption only in girls. Region of residence and age of the mother are significant determinants of wasting in both sexes. Analysis of interaction terms for stunting, however, shows no differences in predictors between boys and girls; only for untimely initiation of breastfeeding do the results for boys (OR 1.46; 95%CI 1.02,2.08) and girls (OR 0.88; 95%CI 0.55,1.41) tend to be different (p=0.12).

Conclusions: In Ethiopia, boys are more malnourished than girls. Exclusive breastfeeding and adequate dietary diversity of complementary feeding are important determinants of stunting in boys and girls. There are no clear gender interactions for the main determinants of stunting and wasting. These findings suggest that appropriate gender-sensitive guidance on optimum infant and young child feeding practices is needed.

Introduction

Globally, stunting – an indicator of chronic undernutrition – affects at least 151 million children under the age of 5 years[1]. The Ethiopia Demographic and Health Survey (DHS) 2016 reports that, despite some improvements in the last 16 years, Ethiopia still displays high rates of childhood malnutrition, with 38% of Ethiopian children under 5 years of age being stunted[2].

Epidemiological studies demonstrate that stunting is frequently associated with repeated exposure to poor sanitation and hygiene; and individual factors such as a child's gender, poor economic conditions[3,4], child morbidity[4,5], and inadequate infant and young child feeding (IYCF) practices[6] have been identified as immediate causes of child stunting. For example, a too early introduction of solid foods before 6 months of age has a significant association with long-term deterioration of physical growth[7], and delaying the introduction of complementary food (CF) is associated with a lower body mass index (BMI) in childhood[8].

Recent studies from several countries worldwide show a higher prevalence of stunting in boys compared to girls[9-11]. In Senegal and Guatemala, the observed gender difference in stunting prevalence is attributed to differential feeding practices, with boys starting complementary feeding at an earlier age, i.e. 2–3 months of age, thereby reducing the period of exclusive breastfeeding[9,11]. A study from South West Uganda reports that stunted children are significantly less likely to be introduced to CF at an appropriate age[10].

Little is known about the existence of gender differences in nutritional status and underlying IYCF practices in Ethiopian infants. Hence, current health promotion activities do not take gender into account. Thus, the aim of our study is to compare the prevalence and potential determinants of stunting between boys and girls. IYCF practices, dietary intake, and maternal and household characteristics are the main determinants investigated. The determinants of wasting as an important indicator of acute malnutrition in young children are also compared between boys and girls.

Methods

This cross-sectional study was performed using the baseline data for a large effectiveness study on the use of multiple micronutrient powders (MNPs) within a local CF programme on iron status, morbidity, and children's growth. Methods and findings of the MNP effectiveness study are described in detail elsewhere[12].

Study area and population

The baseline data collection took place in the Oromia and Southern Nations, Nationalities, and Peoples (SNNP) regions of Ethiopia between March and April 2015. Both regions were selected because of their similar characteristics in food security, child health and nutrition status, and infant feeding practices[13]. The study population consisted of young children 6–11 months of age[12]. Details on the study site and sample selection are described elsewhere[12].

Sample selection

A total of 2356 children from 35 *kebeles*/clusters (the smallest administrative unit in Ethiopia) of 9 *woredas* (districts) were screened and admitted to the study[12]. A child could participate in the study if he/she was ≥6 and <12 months old on the recruitment day and living in one of the selected *kebeles*. Participating children also had to be free from chronic conditions such as metabolic or neurological disorders that might impact their health (e.g. mental retardation). Exclusion criteria included the presence of serious disabilities that would affect normal growth and development. In addition, children with a severe or protracted illness for which continuous medication is required and children with severe malnutrition (weight-height-z score (WHZ) < -3 SD) were excluded from the study and referred to the nearest health facility. In total, 320 children were excluded, and the analyses were performed on data for 2036 children.

Data collection and measurements

Procedures

Three data collectors were assigned to work on a study area of three *kebeles* as a field team. Thirty-six data collectors and six field supervisors were trained in the administration of questionnaires (IYCF, 24 hr recall, and morbidity) and anthropometric measurements. After nine days of training on methodological procedures and quality assurance, the questionnaires were tested in a pilot group and adapted based on the received feedback from the survey team. The questionnaires were translated into local languages (Oromifa and Amharic) and back-translated to English to ensure the quality of the translation. The data collectors' measurements were standardized to ensure that the inter-observer variability was within tolerable limits. Supervisors received additional training on teamwork and on monitoring and supervising the data collection process. The field teams were provided with training and data collection manuals, a chart for calculating age in months, an event calendar, and a WHO classification table for WHZ to identify severely malnourished children. Data were collected at the *kebeles*' health posts by interviewing the child's mother/primary caregiver and taking anthropometric measurements. The supervisors monitored the measurements in order to ensure the quality of the data.

Anthropometric measurements (length and weight) were taken following standard procedures[14]. Weight was measured using the UNICEF Seca 874 U electronic scales (UNICEF Supply

Division, Copenhagen, Denmark) with 100g precision calibrated daily with a known weight, and height was measured on UNICEF's standard measuring board (precision of 0.1cm). All children were measured lying down. Measurements were taken in duplicate and repeated a third time if the difference between the first two was more than 0.5cm or 0.5kg. IYCF practices and morbidity status were assessed using a questionnaire based on WHO recommendations to collect data for the IYCF indicators[15]. A 1-day non-quantified 24hr dietary recall was collected, including information on the source of food, method of preparation, and meal description to assign all ingredients to the respective food groups consumed by the child in the previous 24hr period.

Data processing and analysis

Data processing

All the questionnaires were manually checked for completeness before data entry. Data were coded in duplicate and analysed using SPSS (Version 22.0 for Windows, IBM, New York, USA). The data were cleaned for inconsistencies and missing values. If inconsistencies and missing values could not be resolved by checking the original questionnaires, those data were excluded from further analysis. Children's age was entered as the date of birth provided by the caregivers. Height-for-age (HAZ) and WHZ were determined using the WHO Anthro software version 3.2.2[16] based on the WHO reference population (2006). Stunting was defined as HAZ <-2 of the standard deviation (SD) and wasting was WHZ <-2 SD. IYCF indicators were calculated following the UNICEF guidelines[17]. For the purpose of this study, we defined as 'timely introduced to CF' a) children aged 6–8 months who were fed breastmilk and had had at least one solid or semi-solid food the previous day or b) children aged 9–11 months who had a recall age of the first introduction of CF between 6 and 8 months of age. The seven food groups described by the WHO[17] were used to classify foods consumed, namely: 1) grains, roots, and tubers; 2) legumes and nuts; 3) dairy products; 4) flesh foods; 5) eggs; 6) vitamin A-rich fruits and vegetables; 7) other fruits and vegetables. Minimum dietary diversity was defined as the consumption of four or more food groups from the seven food groups[17]. Minimum meal frequency was defined as the consumption of 2 or more (at age 6–8 months), 3 or more (at age 9–23 months) solid or semi-solid feeds for breastfeeding children, or 4 or more solid or semi-solid or milk feeds for non-breastfeeding children at age 6–23 months[17]. Minimum acceptable diet was defined as a combination of minimum dietary diversity and meal frequency[17]. Basic drinking water and adequate sanitation facilities were defined according to UNICEF and WHO's joint monitoring programme WASH targets and indicators post-2015[18].

Statistical analysis

Child characteristics, i.e. age, height, weight, HAZ, WHZ, stunting, wasting, and IYCF indicators, mother/caregiver characteristics including mother's age, marital status, maternal education and occupation, and household characteristics, i.e. water, sanitation, and hygiene (WASH) indicators and region of residence, were compared between boys and girls using Chi-square tests for categorical variables and Student t-tests for continuous variables.

Binary logistic regression was used to investigate the association between potential determinants and stunting and wasting. Variables associated with the outcome at $p<0.2$ were selected for multiple logistic regression, stratified by gender and adjusted for age, *kebele* (cluster), and mother's characteristics. The interactions between each variable and gender were tested with cross-product terms. For continuous variables (HAZ and WHZ), multiple linear regression was performed including independent variables associated with the outcome in unadjusted analyses at $p<0.2$. A p-value of <0.05 was considered significant. For the tests of interaction terms, a p-value of <0.2 was considered relevant[19].

Ethics approval and consent to participate

Ethical approval was obtained from the Ethiopian National Research Ethics Review Committee, Ministry of Science and Technology, reference number 3.10/865/07. Written permission was also obtained from the Regional Health Bureau of Oromia and SNNP regions, the zonal, *woreda*, and *kebele* offices, before starting the data collection. In addition, permission was received from local leaders in the study area. Detailed information on the purpose of the survey was provided to the mothers/caretakers, both orally and in writing (including a brochure in a local language about the study). Signed consent was obtained from mothers/caregivers of the study children before participation in the study. The study is registered at http://www.clinicaltrials.gov/ with clinical trials identifier of NCT02479815.

Results

The study participants' (n=2036) characteristics are summarized in Table 1. The average age of children was 8.2±1.7 months. An almost equal proportion of male (51.5%) and female (48.5%) children were included. Socio-demographic characteristics were not different between boys and girls. The average age of mothers was 25.4±5.7 years. Almost half of the mothers were illiterate; among literate mothers, a majority (43.8%) had attended primary school (grades 1–8) only. Most households had adequate sanitation facilities and basic drinking water sources.

Stunting and wasting prevalence was significantly higher among boys than girls (18.7% vs. 10.7%, $p<0.001$, and 7.9% vs. 5.4%, $p<0.026$, respectively, Table 1), and girls had a significantly higher HAZ and WHZ than boys. Stunting and wasting increased as the children's age increased (Figure 1, A and B).

In total, 28.3% of young children were reported as having diarrhoea the week before the survey, and 25.5% were reported as having had a common cold or flu, with similar results for boys and girls (Table 1).

More than 75% of mothers started breastfeeding their new-born within one hour of birth (Table 2). Most children, 77% of boys and 78.2% of girls, were exclusively breastfed during the first 6 months of life. Only 5.9% of boys and 7.8% of girls consumed a minimum acceptable diet (MAD), and 6.2% of the boys and 7.8% of the girls met the minimum dietary diversity (MDD) cut-off.

We examined gender differences in the consumption of seven selected food groups (Table 3). Most children (>76%) had consumed cereals and roots/tubers during the previous 24 hr. The consumption of legumes/nuts and eggs was low but increased slightly with age, with the highest consumption of legumes/nuts in boys aged 9–11 months (45.4%); this was significantly higher than the consumption of legumes/nuts in girls of that same age.

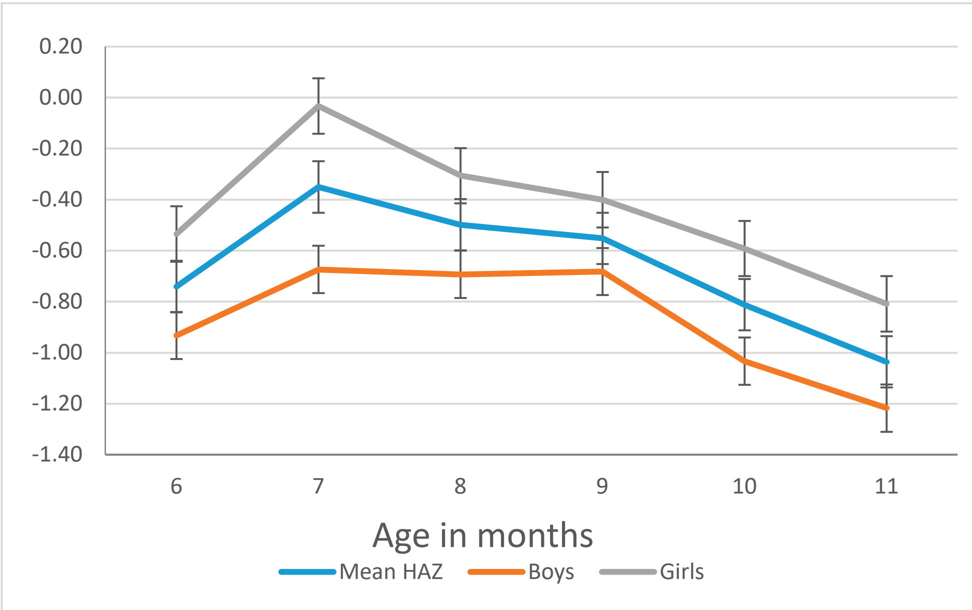
Use of fruits and vegetables tended to be lower in the older boys compared to the girls (19.7% vs 25.0%, p=0.057), whereas the consumption of eggs tended to be higher in older girls compared to boys (25.2% vs 20.5%, p=0.099). The consumption of flesh foods was negligible. There were no significant differences in the consumption of any of the other food groups between boys and girls.

Table 1. Selected socio-demographic, nutritional, and morbidity characteristics of the study population of boys and girls aged 6 to 11 months in two regions in Ethiopia

Characteristics	Total population n =2036	Boys n=1049	Girls n=987	*p*-value†
Region, Oromia %	47.6	53.7	46.3	0.069
Child characteristics				
Child's age in months, mean ± SD	8.2±1.7	8.2±1.7	8.2±1.7	0.459
6–8 n (%)	113 (54.7)	562 (53.6)	551 (55.8)	0.327
9–11.9 n (%)	923 (45.3)	487 (46.4)	436 (44.2)	
Male child, n (%)	1049 (51.5)			
Height, mean ± SD, cm	68.4 ±3.8	68.9 ±3.8	67.9 ±3.8	<0.001
Weight, mean ± SD, kg	7.72 ±1.1	7.9 ±1.1	7.5 ±1.0	<0.001
Height-for-age z score (HAZ), mean ± SD	-0.65±1.4	-0.86±1.4	-0.43± 1.3	<0.001
Stunted (<-2SD) %	14.8	18.7	10.7	<0.001
Severely stunted (<-3SD) %	3.9	6.0	1.7	<0.001
Weight-for-height z score (WHZ), mean ± SD	-0.37±1.1	-0.43±1.1	-0.30±1.1	0.011
Wasted (<-2SD) %	6.7	7.9	5.4	0.026
Diarrhoea (prior 1 wk) %	28.3	28.2	28.4	0.961
Common cold or flu (prior 1 wk) %	25.5	26.0	25.0	0.612
Mother's characteristics				
Mother's age in years, mean (SD)	25.4 ±5.7	25.5±5.9	25.4±5.4	0.903
Mother's educational status %				
Illiterate/none–formal education	48.4	48.8	48.0	0.374
Grades 1–8	43.8	42.8	44.8	
Grade 9 and above	7.8	8.4	7.2	
Marital status %				
Married	96.4	96.3	96.6	0.812
Single/separated/divorced/widowed	3.6	3.7	3.4	
Mother's occupation %				
Housewife/live with family	80.9	80.4	81.6	0.499
Working mother[1]	19.1	19.6	18.4	
Household characteristics[2]				
WASH indicators				
Adequate sanitation %				
Adequate [3]	93.9	94.3	93.5	0.517
Drinking water [4]				
Basic drinking achieved	92.7	93.2	92.1	0.349
Farmland ownership %	91.2	90.1	92.3	0.149

† Chi-square tests were used for categorical variables and Student t-tests (sig 2-tailed) were used for continuous variables to compare the characteristics between boys and girls
[1] Working mother includes farmer, trader, merchant, civil servant, and teacher
[2] n=2023 (undefined n=13)
[3] Adequate sanitation includes a pit latrine with a superstructure, and a platform or squatting slab constructed of durable material; inadequate sanitation includes open pit, shared facilities of any type, no facilities, bush or field[18].
[4] Basic drinking water includes piped water with the subcategories public tap and private tap, protected spring, protected well, water from borehole, water from tanker truck, and rainwater; inadequate basic drinking water: surface water, river, unprotected spring[18]

A



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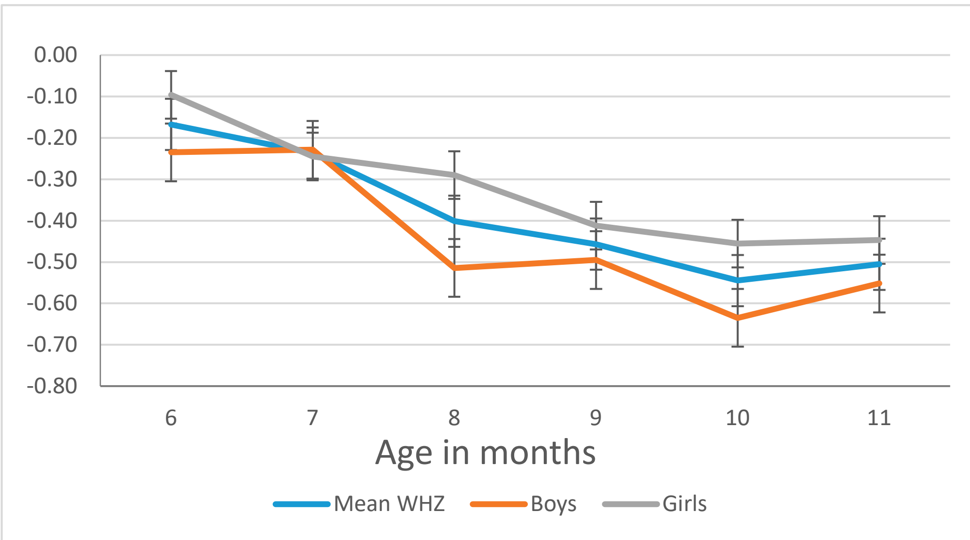

Figure 1. Stunting (HAZ) (A) and wasting (WHZ) (B) in young children (n=2036) aged 6 to 11 months by age and by gender in two regions in Ethiopia

Table 4 describes the factors associated with stunting and wasting. Gender was a significant determinant of nutritional status (odds ratio (OR) for boys vs girls: 1.91 (95%CI 1.48, 2.46) for stunting and OR 1.51 (95%CI 1.06,2.16) for wasting). In addition to gender, of the 18 characteristics investigated, the following were significantly associated with stunting: region of residence, exclusive breastfeeding, timely introduction of CF, diarrhoea during last 7 days, consumption of legumes/nuts, consumption of eggs, and maternal education. Determinants of wasting included region of residence, consumption of legumes and nuts, consumption of other fruits and vegetables, age of the mother, and education of the mother.

Table 2. IYCF practices in boys and girls aged 6 to 11 months in two regions in Ethiopia

	Total population n= 2036	Boys n=1049	Girls n=987	*p*-value
IYCF indicators				
Initiation of BF<1 hr %	75.7	76.9	74.5	0.196
Currently breastfeeding (CBF) %	99.7	99.8	99.5	0.275
Exclusive BF (EBF) at least 6 m %	77.6	77.0	78.2	0.524
EBF in months, mean ± SD	5.9 ± 1.2	5.9 ± 1.4	5.8 ± 0.8	0.344
Introduction to soft and semi-solid foods				
Age (m) CF introduced[1], mean ±SD	5.9 ± 1.2	5.9 ± 1.3	6.0 ± 1.2	0.206
Introduction CF (6–8 months)[2] %	87.2	87.3	87.0	0.894
Minimum dietary diversity (MDD)[3] %	7.0	6.2	7.8	0.164
Minimum meal frequency (MMF)[4] %	75.3	74.8	75.9	0.607
Minimum acceptable diet (MAD)[5] %	6.8	5.9	7.8	0.095

CBF: currently breast feeding (at the time of the survey); m= months; EBF: exclusive breast feeding; BF: breastfeeding; MDD: minimum dietary diversity; MMF: minimum meal frequency; MAD: minimum acceptable diet

[1] n=1998: Boys n=1031, Girls n=967

[2] Received CF: children from 6 to 8 months who received solid, semi-solid, or soft foods in addition to breastfeeding

[3] Minimum dietary diversity: consumption of 4 or more food groups from the 7 food groups, namely: grains, roots, and tubers; legumes and nuts; dairy products (milk, yogurt, cheese); flesh foods (meat, fish, poultry, liver/organ meats); eggs; vitamin A-rich fruits and vegetables; and other fruits and vegetables

[4] Minimum meal frequency: consumption of 2 or more (at age 6–8 months), 3 or more (at age 9–23 months) solid or semi-solid feeds for breastfeeding children, or 4 or more solid or semi-solid or milk feeds for non-breastfeeding children at age 6–23 months

[5] Minimum acceptable diet: a combination of minimum dietary diversity and meal frequency

Table 3. Food group use (%) by gender and age in 6–11 months old children in two regions in Ethiopia

	6–8months (n=1139)			9–11months (n=923)		
Food groups†	Boys n=562	Girls n=551	*p*-value‡	Boys n=487	Girls n=436	*p*-value‡
Cereals and roots/tubers	76.9	78.8	0.471	90.1	89.9	0.913
Legumes and nuts	26.5	28.7	0.422	45.4	38.5	0.039
Dairy	32.9	34.7	0.568	31.6	33.7	0.527
Flesh foods	0	0	-	0.2	0	1.000
Eggs	18.9	20.5	0.498	20.5	25.2	0.099
Vitamin A-rich fruits and vegetables	4.6	4.9	0.888	4.3	5.0	0.641
Other fruits and vegetables	19.0	20.5	0.548	19.7	25.0	0.057

† Calculated on the basis of consumption of the food group in the previous 24hrs
‡ Chi-square tests were used to compare between boys and girls

Chapter 2

Table 4. Factors associated with stunting and wasting in children aged 6 to 11 months in two regions in Ethiopia (n=2036)

Variables	Stunting[1] OR (95%CI)[3]	*p*-value	Wasting[2] OR (95%CI)	*p*-value
Child characteristics				
Region (Oromia†)	1.39 (1.08,1.78)	0.010	0.35 (0.24,0.52)	<0.001
Sex (Female†)	1.91 (1.48,2.46)	<0.001	1.51 (1.06,2.16)	0.022
Age (month)	1.06 (0.98,1.14)	0.133	0.77 (0.54,1.09)	0.138
IBF (before 1hr†)	1.22 (0.93,1.61)	0.158	1.00 (0.67,1.50)	1.000
EBF (yes†)	1.56 (1.19,2.05)	0.001	1.03 (0.68,1.55)	0.908
Timely introduced to CF (yes†)	1.89 (1.38,2.60)	<0.001	1.19 (0.73,1.94)	0.500
MDD (yes†)	1.30 (0.77, 2.20)	0.321	1.41 (0.65,3.08)	0.389
MMF (yes†)	1.17 (0.89,1.54)	0.276	0.90 (0.59,1.36)	0.602
MAD (yes†)	1.27 (0.75, 2.14)	0.372	1.38 (0.63,3.00)	0.423
Diarrhoea last 7 days (no†)	1.31 (1.01,1.70)	0.044	1.10 (0.75,1.61)	0.619
Consumed legumes and nuts (yes†)	1.42 (1.08, 0.93)	0.012	0.64 (0.45,0.91)	0.012
Consumed eggs (yes†)	1.41 (1.02,1.95)	0.038	0.82 (0.55,1.24)	0.345
Consumed other fruits and vegetables (yes†)	0.87 (0.65,1.17)	0.361	1.67 (1.02,2.75)	0.042
Mother's characteristics				
Age of mother (>25 years†)	1.01 (0.79,1.30)	0.929	0.60 (0.42,0.85)	0.004
Education (literate†)	1.32 (1.03,1.69)	0.027	1.42 (1.00,2.02)	0.049
Marital status ([4]†)	0.61 (0.34,1.07)	0.086	0.49 (0.24,1.01)	0.054
Occupation ([5]†)	0.75 (0.54,1.05)	0.095	1.46 (0.97,2.18)	0.069
HH characteristics				
Basic drinking water *(yes†)*	0.83 (0.50,1.36)	0.458	0.47 (0.19,1.16)	0.099
Adequate sanitation *(yes†)*	0.78 (0.45,1.36)	0.378	1.55 (0.83,2.88)	0.171

OR: odds ratio; CI: confidence interval; IBF: initiation of breastfeeding; MDD: minimum dietary diversity; MMF: minimum meal frequency; MAD: minimum acceptable diet; EBF: exclusive breastfeeding; Timely introduced to CF: introduced to complementary food at 6–8 m; HH: household
[1] Stunted n=302, Not stunted n=1734
[2] Wasted n=136, Not wasted n=1900
[3] Univariate analysis was run using logistic regression with stunting or wasting as dependent variable and each variable as independent variable
[4] Single/separated/widowed/divorced
[5] Housewife
† Reference category

We further explored factors associated with stunting (Table 5) and wasting (Table 6) separately for boys and girls, taking age, cluster, and characteristics of the mother and/or household into account. In boys, independently increased odds of stunting were observed for residing in SNNP, late initiation of breastfeeding, non-exclusive breastfeeding until age 6 months, untimely introduction to CF, absence of consumption of legumes/nuts, and illiterate mother. Among girls, only untimely CF introduction, the absence of legumes/nut use, and non-use of eggs were significantly associated with the presence of stunting.

Regarding wasting, for both boys and girls, the region of residence and age of the mother were the only significantly independent risk factors, with lower odds of wasting when residing in SNNP (compared to Oromia) and when having a mother > 25 years of age (Table 6). Consumption of legumes and mother's marital status tended to be significant determinants for wasting in boys ($p<0.10$) but not in girls, whereas absence of adequate sanitation tended to be significant in girls but not in boys.

The interaction terms between gender and all main determinants were tested in additional logistic regression analyses. There was an indication of an interaction between early initiation of breastfeeding and gender ($p=0.128$), suggesting that the association between initiation of breastfeeding and stunting was different between boys and girls. No clear interactions with sex were observed for the other variables, neither for stunting nor for wasting (see Supplemental Table I).

Table 5 Determinants of stunting among boys (n=1049) and girls (n=987) adjusted for age, cluster, and mother's characteristics in two regions of Ethiopia

Variables	Boys AOR (95%CI)	*p*-value	Girls AOR (95%CI)	*p*-value
Child characteristics				
Region (Oromia†)	2.00 (1.41,2.83)	<0.001	1.52 (0.98,2.36)	0.060
Age (month[1])	1.07 (0.98,1.18)	0.140	1.02 (0.90,1.15)	0.752
IBF (before 1hr†)	1.46 (1.02, 2.08)	0.037	0.88 (0.55,1.41)	0.589
EBF (yes†)	1.66 (1.17,2.35)	0.004	1.28 (0.81,2.04)	0.294
Timely introduced to CF (yes†)	2.14 (1.40,3.27)	<0.001	1.85 (1.09,3.15)	0.024
Diarrhoea last 7 days (no†)	1.27 (0.90,1.78)	0.172	1.44 (0.94,2.21)	0.096
Consumed legumes and nuts (yes†)	1.45 (1.02,2.06)	0.037	1.86 (1.15,3.00)	0.011
Consumed eggs (yes†)	1.21 (0.80,1.83)	0.363	1.76 (1.00,3.08)	0.049
Mother's characteristics				
Education (literate†)	1.44 (1.05,1.97)	0.023	1.22 (0.82,1.84)	0.329
Marital status[2†]	0.62 (0.29,1.31)	0.209	0.44 (0.17,1.11)	0.081
Occupation[3†]	0.65 (0.43,1.00)	0.051	0.73 (0.42,1.28)	0.278

AOR: adjusted odds ratio; *CI:* confidence interval; IBF: initiation of breastfeeding; EBF: exclusive breastfeeding; Timely introduced to CF: introduced to complementary food at 6–8 m;
† Reference category
[1] Adjusted for cluster only and mother's characteristics
[2] Single/separated/widowed/divorced
[3] Housewife

Determinants were also investigated in relation to HAZ and WHZ as continuous outcome variables (see Supplemental Table II). Boys had a lower HAZ than girls, and HAZ decreased with age, was lower in those with untimely introduction of CF, not consuming legumes and nuts and not consuming eggs, and having a mother or caregiver < 25 years of age. WHZ was lower in Oromya in boys;

decreased with age; and was lower in those with low MDD, in the presence of diarrhoea, in older mothers or caregivers, in nonworking mothers, and from a household with inadequate sanitation.

Discussion

Our analyses show that gender differences in stunting and wasting exist in Ethiopian infants aged 6–11 months, with boys being 1.9 times more likely to be stunted and 1.5 times more likely to be wasted than girls. Risk factors for stunting and wasting are not significantly different between boys and girls, although small differences exist. Region of residence, untimely initiation of breastfeeding, exclusive breastfeeding, and low maternal education are significant risk factors for stunting in boys. Untimely introduction to complementary food and low consumption of legumes/nuts are significant risk factors for stunting in both boys and girls, and only in girls is low egg consumption associated with stunting. Region of residence and mother's age are the significant independent predictors of wasting in both sexes.

The gender differences that we observed in nutritional status are consistent with findings from the northern part of Ethiopia[20] as well as from some other Sub-Saharan African countries[10,21-25]. A meta-analysis of 16 demographic and health surveys from 10 Sub-Saharan African countries in 2007 also shows that male children were 1.16 times more likely to be stunted than females[26]. A recent meta-analysis of data on children (6–59 months) from 84 countries in 2018 also reports a similar trend of a significantly higher prevalence of stunting (34.3% vs 31.7%) and wasting (9.5% vs 8.1%) among boys compared to girls[27].

Table 6 Determinants of wasting among boys (n=1049) and girls (n=987) adjusted for age, cluster, and mother's characteristics in two regions of Ethiopia

Variables	Boys AOR (95%CI)	Boys *p*-value	Girls AOR (95%CI)	Girls *p*-value
Child characteristics				
Region (Oromia†)	0.45(0.26,0.78)	0.004	0.38(0.19,0.75)	0.006
Age (month)[1]	1.11(0.98,1.27)	0.110	1.03(0.87,1.21)	0.755
Consumed legumes and nuts (yes†)	0.66(0.41,1.06)	0.088	0.86(0.48,1.54)	0.605
Consumed other fruits and vegetables (yes†)	1.40(0.74,2.66)	0.305	1.83(0.81,4.15)	0.150
Mother's characteristics				
Age of mother (>25 year †)	1.68 (1.04,2.73)	0.035	1.79(1.00,3.21)	0.051
Education (literate†)	1.09(0.67,1.76)	0.741	1.55(0.85,2.80)	0.150
Marital status[2†]	0.43(0.17,1.07)	0.070	0.54(0.15,1.90)	0.335
Occupation[3†]	1.15(0.67,1.98)	0.623	1.59(0.84,3.01)	0.155
HH characteristics				
Basic drinking water(yes†)	0.30(0.07,1.26)	0.101	0.69(0.21,2.27)	0.537
Adequate sanitation (yes†)	0.97(0.37,2.53)	0.955	2.02(0.86,4.74)	0.106

AOR: adjusted odds ratio; *CI:* confidence interval
† Reference category;
1 Adjusted for cluster and mother's characteristics
2 Single/separated/widowed/divorced
3 Housewife

Although poor IYCF practices were observed in both boys and girls, our multivariate analysis shows that risk factors for stunting are not completely similar for each gender. Variation in the initiation of breastfeeding and exclusive breastfeeding are significant independent determinants of stunting in boys, but not in girls, suggesting a higher vulnerability to poor feeding practices among boys compared to girls in the first months of life. In contrast, timely introduction to CF is a common determinant of stunting for both boys and girls.

Several possible explanations are reported in relation to gender differences in nutritional status. First of all, these differences might result from biological differences that could be independent of infant feeding patterns[9]. For instance, boys are more susceptible to infectious diseases[26] and show higher biological fragility in the first year of life[28]. However, the underlying mechanisms for the biological difference are poorly understood[26]. Secondly, a study in Madagascar[29] found that gender differences in stunting tend to vary with age, with males more likely to become stunted in the first year, whereas females are more likely to become stunted in the second year of life[30]. Our study included only children in the first year of life, and this could partly explain the higher stunting rates in boys.

The high morbidity observed in our study may be associated with a high number of illiterate mothers in the study regions. The finding of the association between increased risk of morbidity and mother's illiteracy are consistent with findings of studies conducted in rural Ethiopia[31] and Tanzania[32]. Our results show that the mother's literacy status and maternal occupation are two of the independent determinants of stunting in boys but not in girls. Studies in Southern Ethiopia[33], Mozambique[25], and Bangladesh[34] also found the mother's literacy status to be associated with stunting. Literacy status may be indicative of a mother's better knowledge and awareness of child nutrition and may therefore result in relatively better feeding practices[34].

One of the main findings of this study is that region of residence is a determinant of stunting and wasting independent of the other determinants. We observed regional differences in stunting and wasting, where stunting is higher (OR 1.39) but wasting lower (OR 0.35) in SNNP compared to Oromia. In the Ethiopia 2016 DHS, a similar trend was observed for stunting (38.6% vs 36.5%) and for wasting (6.0% vs 10.6%) in SNNP versus Oromia, respectively, for children under 5 years of age[2]. A recent meta-analysis conducted in Sub-Saharan Africa also shows regional differences in stunting patterns and suggests the importance of contextualizing appropriate nutrition interventions[35,36].

A limitation of this study is that it uses the baseline data of an intervention study, with one of the inclusion criteria being WHZ > -3 SD. This means that we cannot exclude the possibility that the results, of for example differences between regions, might have been different if severely stunted children had been included.

The main strength of the study is that it involves a large sample size that represents the target population in the two largest regions of the country and an area where nutritional improvements are needed. Secondly, the study team underwent 9 days of intensive training, including standardization of data collectors and pilot testing of the questionnaires, which helped to refine the questionnaires and avoid questions that might lead to biased answers[37]. This reduced the measurement error that can occur during data collection if measurements are collected differently in exposure and outcome. To our knowledge, this is the first study to assess gender differences in determinants of nutritional status in these regions in Ethiopia with such a large sample size (n=2036).

Even though the selected *woredas* are UNICEF's Community-Based Nutrition (CBN) *woredas*, which presumably have better Infant and Young Child Nutrition (IYCN) programmes, the observed IYCF practices are suboptimal; this partly suggests that these *woredas* have been correctly targeted, as the worst-off *woredas* are more eligible for CBN interventions. However, it also suggests the need for more efforts to strengthen the ongoing IYCN programmes within the CBN *woredas*. An ethnographic study on gender-related maternal beliefs and attitudes regarding IYCF practices would help to better clarify the underlying causes of the observed gender differences and the differences in vulnerability of the two sexes during infancy. In addition, there is emerging evidence that early life nutrition may affect the development of chronic diseases differently in boys than in girls[38]. For instance, birth weight has been found to predict the risk of insulin resistance later in life in men, but not in women[38]. Therefore, the observed gender differences in early life nutrition may have long-term health implications and need to be addressed[38].

Conclusion

In conclusion, the results of this study show that gender differences in nutritional status exist in Ethiopia: girls have a better nutritional status compared to boys during the first year of life. Determinants of stunting and wasting are largely similar between the sexes, although poor breastfeeding practices in the first 6 months of life seemed to affect stunting more in boys than in girls. Exclusive breastfeeding and adequate dietary diversity of complementary feeding are important determinants of stunting in boys and girls. The findings of this study will contribute to the development of gender-sensitive behaviour change intervention materials that would contribute to the effort to convince and guide mothers to introduce complementary foods in a timely fashion, regardless of the child's gender.

List of abbreviations

BF: breastfeeding, CBF: current breastfeeding; CF: complementary food; CI: confidence interval; cm: centimetre; EBF: exclusive breastfeeding; EPHI: Ethiopian Public Health Institute; HAZ: height-for-age Z score; IBF: initiation of breastfeeding; IYCF: infant and young child feeding; IYCN: infant and young child nutrition; MAD: minimum acceptable diet; MDD: minimum dietary diversity; MMF: minimum meal frequency; NI: Nutrition International; SD: standard deviation; SNNPR: South Nations, Nationalities, and Peoples Region; SPSS: Statistical Package for the Social Sciences; UNICEF: United Nation Children's Fund; WASH: Water, Sanitation, and Hygiene; WHZ: weight-for-height z score; WHO: World Health Organization.

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Chapter 2

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Supplemental Tables

Supplemental Table 1. Results for testing interaction terms between gender and other determinants of stunting (see Table 5) and wasting (see Table 6) (n=2036)[1] in two regions of Ethiopia

Variables	Stunting Exp(β) (95%CI)	*p*-value	Wasting Exp(β) (95%CI)	*p*-value
Child characteristics				
Region (Oromia†)	0.76(0.45,1.27)	0.289	1.50(0.68,3.29)	0.317
Age (month)	1.04(0.90,1.21)	0.583	0.93(0.75,1.15)	0.494
IBF	1.57(0.88,2.82)	0.128	‡	
EBF	1.27(0.71,2.25)	0.418	‡	
MDD	‡		‡	
MMF	‡		‡	
MAD	‡		‡	
Timely introduced to CF	1.12(0.58,2.18)	0.732	‡	
Diarrhoea last 7 days	0.90(0.52,1.54)	0.689	‡	
Consumed legumes and nuts	0.79(0.45,1.41)	0.429	1.26(0.61,2.59)	0.537
Consumed eggs	0.70(0.35,1.38)	0.302	‡	
Consumed other fruits and vegetables	‡		0.99(0.43,2.27)	0.987
Mother's characteristics				
Age of mother (>25 year†)	‡		1.12(0.55,2.28)	0.764
Education	1.18(0.71,1.96)	0.532	1.34(0.65,2.76)	0.427
Marital status	1.20(0.37,3.84)	0.763	1.26(0.28,5.74)	0.765
Occupation	0.84(0.42,1.67)	0.617	1.47(0.65,3.33)	0.361
HH characteristics				
Basic drinking water	‡		0.47(0.07,2.99)	0.421
Adequate sanitation	‡		0.45(0.13,1.60)	0.220

Exp(β): odds ratio; CI: confidence Interval; IBF: initiation of breastfeeding; EBF: exclusive breastfeeding; MDD: minimum dietary diversity; MMF: minimum meal frequency; MAD: minimum acceptable diet; Timely introduced to CF: introduction to complementary food at 6–8 m; HH: household

1 Interaction was evaluated (each variable+ gender + gender*each variable) using logistic regression; a $p<0.2$ was considered relevant for interaction terms

† Reference category

‡ Not included in Tables 5 or 6

Supplemental Table 2. Multiple predictors [1]of HAZ and WHZ in children aged 6–11 months (n=2035) in two regions of Ethiopia

	Height for Age (HAZ)		Weight for Height (WHZ)	
Variables	**β(SE)**	***p*-value**	**β(SE)**	***p*- value**
Intercept	-0.31(0.16)	0.046	-0.14(0.14)	0.315
Child characteristics				
Region (SNNP†)	0.07(0.06)	0.249	-0.23(0.06)	<0.001
Sex (Female†)	-0.42(0.06)	<0.001	-0.11 (0.05)	0.017
Age (month, 11 m†)				
6 months	0.39(0.11)	<0.001	0.35(0.09)	<0.001
7 months	0.71 (0.12)	<0.001	0.23(0.10)	0.015
8 months	0.51 (0.12)	<0.001	0.11(0.10)	0.263
9 months	0.47 (0.12)	<0.001	0.08(0.09)	0.381
10 months	0.17 (0.12)	0.156	-0.02(0.09)	0.860
IBF (before 1 hr†)	-0.03(0.07)	0.647	‡	
EBF (yes†)	-0.15(0.08)	0.069	‡	
MDD (yes†)	-0.13(0.13)	0.318	-0.26(0.10)	0.007
MMF (yes†)	‡		-0.07(0.06)	0.234
Timely introduced to CF (yes†)	-0.45(0.10)	<0.001	‡	
Diarrhoea last 7 days (yes†)	‡		0.23(0.06)	<0.001
Consumed legumes and nuts (yes†)	-0.17(0.07)	0.013	‡	
Consumed eggs (yes†)	-0.17(0.08)	0.032	‡	
Consumed other fruits and vegetables (yes†)	‡		0.001(0.07)	0.983
Mother's characteristics				
Age of mother (>25 years†)	-0.14(0.06)	0.019	0.10(0.05)	0.047
Education (literate†)	‡		-0.06(0.05)	0.237
Marital status[2†]	‡		‡	
Occupation[3†]	‡		0.16(0.06)	0.008
HH characteristics				
Basic drinking water (yes†)	‡		‡	
Adequate sanitation (yes†)	‡		-0.21(0.10)	0.037

β: unstandardized coefficients; SE: standard error; IBF: initiation of breastfeeding; EBF: exclusive breastfeeding; MDD: minimum dietary diversity; MMF: minimum meal frequency; Timely introduced to CF: introduced to complementary food at 6–8 m;
HH: household
[1] Variables included in multiple linear regression are based on simple regression with $p<0.20$
[2] Single/separated/widowed/divorced
[3] Housewife
† Reference category
‡ $p>0.2$ and not included in the model

Chapter 3

Identifying dietary strategies to improve nutrient adequacy among Ethiopian infants and young children using linear modelling

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Abstract

Background:

Optimal Infant and Young Child Feeding practices are crucial for child survival. However, in Ethiopia local food-based dietary guidelines providing guidance on how to ensure nutrient adequacy, do not exist.

Methods:

Nutrient adequacy of young children’s diet was assessed to identify best possible strategies to improve nutrient adequacy. Data from the Ethiopian National Food Consumption Survey were analysed using Optifood (a linear programming software)to identify nutrient gaps in diets for children (6-8, 9-11 and 12-23 months), and to formulate feasible Food- Based Dietary Recommendations (FBDRs) for improved nutrient adequacy in four regions which differ in culture and food practices. Alternative interventions including a local complementary food, micronutrient powders (MNPs), Small quantity Lipid-based Nutrient Supplement (Sq-LNS) and combinations of these were modelled in combination with the formulated FBDRs to compare their relative contributions to improved nutrient adequacy. The risk of inadequate and excess nutrient intakes when MNP was added daily or every other day to observed intakes; was simulated using the Estimated Average Requirement cut-point method and the full probability approach.

Results:

Optimised local diets did not provide adequate zinc in all regions and age groups, iron for infants <12 months of age in all regions, and calcium, niacin, thiamine, folate, vitamin B12 and B6 in some regions and age-groups. The set of regional FBDRs, considerably different for four regions which differ in culture and food practices, increased nutrient adequacy but some nutrients remained sub-optimal.

Conclusions:

Combination of regional FBDRs with daily MNP supplementation for 6-12 months of age and every other day for 12-23 months of age; closed the identified nutrient gaps without leading to a substantial increase in the risk of excess intakes. Regional FBDR needs to be combined with daily (6-12 months) and every other day (12-23 months) MNP supplementation to cover nutrient adequacy together with promotion of breast-feeding on demand during the first two years of age.

Introduction

Ensuring optimal Infant and Young Child Feeding (IYCF) practices has been identified as one of the most effective public health interventions to improve child survival in developing countries[1]. The United Nations International Children's Emergency Fund (UNICEF) and the World Health Organization (WHO) recommend that infants are exclusively breastfed during the first 6 months of life and are given nutrient dense semi-solid or solid complementary foods in addition to continued breastfeeding from the age of 6 months until at least 2 years of age[2]. In its 2003 Global Strategy for IYCF, the WHO emphasizes the use of suitable locally available foods when introducing complementary foods[3]. This recommendation is challenging in a country like Ethiopia, where children transition directly to adult diets that are often monotonous, and primarily composed of low nutrient dense cereal-based foods. Further, any infant-specific foods fed to young children tend to be of low nutrient density[4-7].

According to Ethiopia's 2016 Demographic and Health Survey, more than half of children 6-23 months of age do not achieve the recommended feeding frequency for their age and just 7% of these children consume a minimum acceptable diet (a combination of minimum dietary diversity which is a consumption of four or more food groups from the seven food groups and minimum meal frequency which is consumption of 2 or more (at age 6-8 months), 3 or more (at age 9-23 months) solid or semi-solid feeds for breastfeeding children or 4 or more solid or semi-solid or milk feeds for non-breastfeeding children at age 6-23 months)[8, 9]. Data from the 2011 Ethiopian National Food Consumption Survey (NFCS) reported high intakes of iron across all age groups including children from 1 to 3 years of age[10], whereas intakes of other micronutrients such as zinc and vitamin A were below recommendations. Although several small-scale and short term Infant and Young Child Nutrition programs combining capacity building and behaviour change communication were able to improve IYCF practices in Ethiopia[11, 12], they are limited by the absence of evidence-based, realistic food-based dietary recommendations (FBDR) to guide improved practices.

Linear programming is a mathematical method that has been used to formulate robust FBDR[13-17]. Linear programming has also been used to objectively identify key nutrient gaps in optimised local diets[16, 18-20] and to define "problem nutrients" i.e., nutrients for which it may be difficult to ensure nutrient adequacy with local foods alone[17, 21]. In Ethiopia, the Alive and Thrive programme used linear programming to determine whether micronutrient requirements of breastfed infants (6-8 and 9-11 months) could be met using only unfortified local foods, and illustrated the nutritional needs of infants were difficult to meet when fortified products are not consumed[22]. These analyses, however, were limited to a pilot study conducted in one region, using a list of foods available in markets rather than information on foods that were actually consumed by infants in this region. Also, they did not take into account the regional variability in food consumption patterns in Ethiopia.

To address these limitations, in the current study, we used nationally representative individual dietary intake data from the NFCS[10] in linear programming analyses, to identify "problem nutrients" and formulate realistic FBDRs for young children (6-8, 9-11, and 12-23 months of age) from four regions of Ethiopia. In addition, we modelled various nutrition intervention alternatives that could be used to help improve nutrient adequacy: including a locally produced complementary food (CF), Micronutrient Powders (MNPs)[23] and Small quantity Lipid-based Nutrient Supplements (Sq-LNS)[24, 25]. In addition, we also assessed the risk of inadequate intakes and excess intakes through these interventions.

Methods

Study design

In this secondary data analyses, we used anthropometric and 24-hour dietary recall data collected from a subgroup of 6-23 months old children in the cross-sectional NFCS[10]. The NFCS data were collected between June-September 2011. Ethical approval for the NFCS was obtained from the Scientific and Ethics Review Committee of Ethiopian Public Health Institute (EPHI), reference number EHNRI 6.13/157.

We used linear programming (LP) software (Optifood) to develop Food Based Dietary Recommendations (FBDR), identify nutrient gaps in local diets and test alternative interventions, as reported elsewhere[15, 26, 27]. The LP analyses were done by age group and region to theoretically determine whether (1) FBDR could ensure nutrient adequacy and if not, whether including in the set of FDBRs (2) a locally produced CF consisting of grains and legumes (FBDR + CF), (3) MNP (FBDR + MNP), (4) Sq-LNS (FBDR + Sq-LNS), (5) CF and MNP (FBDR + CF + MNP) or (6) CF and Sq-LNS (FBDR + CF + Sq-LNS) would further improve the nutrient adequacy of young children's diets.

After adjusting the observed nutrient intake distributions for intra-subject variability as described elsewhere[28], the prevalence of inadequate nutrient intakes were assessed using the EAR cut-point method and full probability approach[28, 29]; and the risk of excess intakes was assessed using the tolerable upper intake level. These simulations were done for observed intakes, observed intakes plus daily MNP and observed intakes plus MNP every other day.

Study population

The NFCS is a nationally and regionally representative sample of 6-35 month- old children (n=8079). Our analyses were performed on a subgroup of 31% of these children (n=2498) by only including children within the age range of 6-23 months and residing in four regions Tigray, Amhara, Oromia and South Nations, Nationalities and Peoples Region (SNNPR). These four regions were selected to ensure representation of regions included in the pilot complementary feeding program of Nutrition International (NI) and UNICEF[30]. Moreover, these regions are the largest regions in the country and represent different local cultures and feeding habits.

Data preparation

Data were prepared by region and age group (6-8 months, 9-11 months and 12-23 months). We defined model parameters based on the information on food intakes and recipe composition of NFCS data, using the Optifood data preparation programme in MS Access. Constraints used to ensure realistic modelled diets were defined by (i) the average energy requirement for the target groups, estimated using the FAO/WHO algorithm for energy requirement and the standard average weight for children in each age group as reported by WHO Child Growth Standards: 7.9kg for 6-8months, 8.8kg for 9-11months and 10.5kg for 12-23 months children[31, 32]; (ii) foods commonly consumed by the target population defined as those consumed by more than 3% of the target population, per region and age group, excluding water, condiments and salt. We used 3% because, using foods consumed by >5%[33]we were unable to model the foods in module 1 as the energy ranges were too tight to reach 80% and 120%. Foods with a portion size below 0.5 g/d or consumed with a weekly frequency below 0.5 servings per week were excluded, as only rounded values were used to set model parameters, (iii) the estimated average serving size of those foods, calculated as the daily median intake of foods in gram for only children consuming that particular food, and (iv) the minimum and maximum consumption frequency per week for each food, food group and sub-food group. Foods were assigned to food groups and subgroups. The minimum and maximum frequency of consumption per week of selected food groups and sub food groups were defined as the 10^{th} and 90^{th} percentiles of weekly frequencies, respectively. The median weekly consumption frequency for food groups defined the food pattern goals used in subsequent steps in Optifood. The proportion of children consuming each food was used to estimate the maximum number of servings per week for each food. The reported minimum number of servings/week per food was usually zero except for breast milk intake.

Foods belonging to the food groups' grain and grain products or starchy roots were considered staple foods. Foods consumed only in between meals were considered snacks. The type of meal (snack or staple) was determined based on the nature of the food and time of the food consumption.

As the NFCS did not assess the quantity of breastmilk intake, we assumed an average daily intake of breast milk as reported by WHO for developing countries (660g, 616g and 549g per day for 6-8months, 9-11months and 12-23months children respectively)[21]. Constraints on the minimum and the maximum number of daily servings per week of breastmilk were set at 6.9 and 7.1 respectively. The nutrient composition of breast milk used was derived from WHO[34].

The content of vitamin A, iron, zinc, calcium, protein, fat, carbohydrate of foods consumed, for input data in Optifood, were obtained from the food databases compiled for NFCS 2011, which were primarily from local food composition table (FCT) III and IV[35, 36] and other regional or international published data[10]. Food composition values for vitamin B_6, B_{12} and folate were derived from the USDA food composition database. The FAO/WHO daily nutrient requirements for protein, thiamine, riboflavin, niacin, vitamin B_6, folate, vitamin B_{12}, vitamin C, vitamin A, calcium, iron, and zinc were used[37-39]. Based on the cereal-based dietary pattern with low consumption of animal- derived products and vitamin C, and the extreme low dietary diversity in children[40, 41] we considered low bioavailability (15%) for zinc[10] and 5% bioavailability for iron[10].

To define the nutrient composition of the local CF, which was one of the alternative interventions tested, we used a combination of the most abundant cereals and legumes available in the four study regions of Ethiopia according to an assessment of community-based production of complementary foods in Ethiopia[11]. We estimated the portion size of an average CF serving by identifying portion sizes as estimated by Lutter and Dewey (40g for 6-11 months and 60g for 12-23months)[42] and, verifying these portion sizes for the different age groups with a group of mothers of children aged 12 to 23 months of age participating in an on-going MNP effectiveness study[43]. The nutritional composition used for the local CF per 100 grams is shown in **Table 1**. The Micronutrient Powder (MNP) used in our analyses was the Mix Me® Vitamin and Mineral Powder from DSM Nutritional Products[44]. It contains a mixture of 15 vitamins and minerals in a single dose 1g sachet (Table 1). The Sq-LNS composition used in this study corresponded to the Nutributter® composition from Nutriset. This supplement is formulated for children aged from 6 to 24 months old. The recommended dosage is 20g/day to provide daily needs of 22 vitamins and minerals plus protein and essential fatty acids (Table 1).

Table 1. Nutrient composition of local complementary food per 100 gram and different supplements per serving size, per region.

	CF* Tigray	CF* Amhara	CF* Oromia	CF* SNNPR	MNP**	Sq-LNS***
	100g	*100g*	*100 g*	*100g*	*1g*	*20g*
Energy (kcal)	351	357	371	373	0	118
Protein (g)	13.4	13.1	10.7	11.2	0	2.6
Water (g)	9.8	9	8.0	7.5	0	4
Fat (g)	1.7	2.1	2.8	2.9	0	9.6
Carbohydrate (g)	73.2	73.9	76.4	76.2	0	5.3
Calcium (mg)	57.5	42.8	38.8	27.7	0	280
Iron (mg)	11.9	7.8	10.8	4.7	6	6
Zinc (mg)	1.6	1.7	1.2	1.5	4.1	8
Vitamin C (mg)	0.5	1.4	2.6	3.2	30	30
Thiamin (mg)	0.3	0.3	0.3	0.3	0.5	0.3
Riboflavin (mg)	0.2	0.2	0.1	0.1	0.5	0.4
Niacin (mg)	3.3	2.9	1.5	1.6	6	4
Vitamin B6 (mg)	0.3	0.3	0.3	0.2	0.5	0.3
Folate (µg dietary equivalents)	138.7	130	107.2	103.8	150	80
Vitamin B12 (mg)	0	0	0	0	0.9	0.5
Vitamin A (mg)	0.8	1.5	1.5	1.9	400	400

* CF=Local complementary Food product, ** MNP=MicroNutrient Powder supplement, *** Sq-LNS=Small quantity Lipid base Nutrient Supplement.

Data analyses

The NFCS anthropometric data were analysed using WHO Anthro software version 3.2.2[45] to estimate Z-scores for height-for-age (HAZ), weight-for-height (WHZ) and weight-for-age (WAZ). Children were classified as stunted, wasted and under-weight if their Z-score values for HAZ, WHZ and WAZ were below -2 SD, respectively.

Analysis using linear programming

The linear programming analyses were done per age group (n=3) and per region (n=4) using Optifood [14, 15], thus in total, 12 sets of FBDR were developed. Through Module I we checked whether the entered data produced realistic and feasible diets. Module II formulated two nutritionally "best diets" for each target group to show whether or not realistic combinations of locally available foods could provide the RNIs for all nutrients, identifying nutrient gaps when it was not possible. In Module II, a "food pattern" diet was selected that aimed to achieve both food group pattern and nutrient goals and a "no-food pattern" diet was selected that aimed to achieve only nutrient goals. In module III, two diets per nutrient were modelled of which one minimizes (worst-case scenario) and one maximizes (best-case scenario) the nutrient content of the diet by preferentially selecting respectively the lowest and highest nutrient dense foods for that specific nutrient[15]. Module III was first run without testing any recommendations. If the modelled diets did not reach 70% of the RNI in the "worst-case" scenario but reached 100%RNI for the "best-case" scenario for individual nutrients, then this nutrient was considered a "partial problem" nutrient. If the modelled diets did also not reach 100% of the RNI in the "best-case" scenario for individual nutrients, then this nutrient was considered a "problem" nutrient. Subsequently, recommendations were tested individually in Module III. This comprised including foods (food groups) constraints in the model and then minimizing each nutrient to determine its percentage RNI achieved in the diet with its lowest content. The foods /food group/ food sub-group recommendations tested, in Module III, were selected by examining Module II "best diet-without food pattern goals". Food groups were tested if the modelled diet's pattern was higher than the observed median food group pattern; sub food groups and foods were selected when they contributed > 5 % to at least one of the nutrients in the modelled diet. Individually tested food groups, sub food groups, and foods were combined. Specifically, the combination of food groups, sub food groups, and foods with the highest number of nutrients reaching at least 70% of RNI in the "worst-case" scenario analyses were selected as the baseline FBDR. When the selected baseline FBDR could not ensure nutrients adequacy, 5 alternative options of FBDR were identified and assessed to see whether or not nutrient gaps could be filled. In combination with the FBDRs, the 5 alternative options namely local CF product, MNP, Sq-LNS, CF+MNP and CF + Sq-LNS and the nutrient adequacy of each combination as well as possible modifications in the frequency of alternative options were assessed to present the option that offers the best nutritional profile for each age group and region.

Analysis using the EAR cut-point method and the full probability approach

From NFCS observed data, the prevalence of inadequate and excess intakes were calculated in 3 series of analyses; 1) the adjusted observed dietary intakes, 2) the adjusted observed intakes plus a daily (7 servings/week) or 3) every other day (3.5 servings/week) dosage of MNP. We used the Estimated Average Requirement (EAR) cut-point method for zinc (15% and 30% bioavailability) and the full probability approach for iron using a bioavailability of 5% and 10% for each age group[28, 29]. "Compl-eat© (version 1.0, Wageningen University, The Netherlands)" was used to calculate observed intakes of iron and zinc. Log transformation and square root transformation were used for intakes since nutrient intakes were not normally distributed. Adjusted observed intakes were then determined with the transformed data, using the Ugandan estimates for the within-person variation, since these estimates were not available for Ethiopia[46] and the between-person variation calculated from the NFCS, using the NRC method[47, 48]. The EAR and the tolerable upper intake level (UL) from the Institute of Medicine (IOM)[49] were used for iron except for the EAR of 12-23m which is from WHO/FAO[50]. For zinc, we used the EAR set by IOM[49] for 6-11m and WHO/FAO[50] for 12-23m and, used the UL suggested by WHO[51] as well as the UL suggested by IZiNCG[51], since the two UL cut-offs are quite different.

Results

The socio-demographic characteristics and nutritional status of the study children are presented in **Table 2**. Most children were 12-23 months of age and from rural areas (81-90%). A higher percentage of stunting and underweight were observed in Tigray (43% and 31%) and Amhara (41% and 28%) compared to SNNPR (35 % and 21%) and Oromia (34 % and 26%) respectively. Wasting was highest in Oromia (14%).

Overview of foods consumed

The majority of children in all age groups (>84%) were consuming breastmilk (**Table 3**). Table 3 also summarizes the total number of foods consumed by the study children and number of foods consumed by >3% of children per age group and region. In children 6-8 months of age, on average only 28 foods were consumed by >3% of the population. This increased to 38 food items for 9-11 months old children and 52 food items for 12-23 months old children.

Table 2. Characteristics of study children by age group and region.

Characteristics	Tigray	Amhara	Oromia	SNNPR
Total number	472	659	675	692
6-8 months	89	122	135	151
9-11 months	86	120	129	129
12-23 months	297	417	411	412
Sex (male%)				
6-8 months	43.8	56.2	54.1	48.3
9-11 months	44.2	47.5	59.7	51.9
12-23 months	45.5	51.9	57.3	55.1
Place of residence (%)				
Urban	19.3	13.7	10.4	10.3
Rural	80.7	86.3	89.6	89.7
Nutritional status				
HAZ* (mean ±SD)	-1.73 ±1.39	-1.61±1.79	-1.21±2.00	-1.37±1.72
Stunting (%)	42.6	40.8	33.7	34.9
WAZ** (mean ±SD)	-1.45±1.09	-1.33±1.24	-1.16±1.40	-1.03±1.34
Underweight (%)	30.8	28.2	25.5	20.8
WHZ*** (mean ±SD)	-0.73±1.10	-0.66±1.27	-0.69±1.31	-0.40±1.21
Wasting(%)	11.5	11.7	14.4	8.5

*HAZ-Height for Age Z Score,** WAZ-Weight for Age Z Score,*** WHZ Weight for height Z Score
Stunting defined as HAZ <-2 of the standard deviation (SD), underweight WAZ <-2 SD and wasting WHZ <-2 SD were determined using the WHO Anthro software version 3.2.2.

Chapter 3

The list of foods consumed by >3% of the children including the serving sizes modelled, per age group and region is summarized in **supplemental Table 1**. Among the grains, tef, wheat, sorghum and barley were consumed across all age groups and regions. The most commonly consumed legumes were peas, vetch, chickpeas, broad beans, and kidney beans. Milk was commonly consumed in all regions. It was observed that infants were rarely fed fruits or sweetened snacks, vegetables and eggs.

Table 3. Reported intake and feeding practice by age group and region.

Age group		Tigray	Amhara	Oromia	SNNPR	Average of all regions
6-8 months	Breast milk %	99	97	95	98	97
	Foods consumed (n)	74	82	93	70	80
	Foods consumed by >3% of children(n)	28	26	24	33	28
9-11 months	Breast milk%	95	93	89	94	93
	Foods consumed (n)	78	99	100	94	93
	Foods consumed by >3% of children(n)	29	35	40	47	38
12-23 months	Breast milk%	86	90	85	91	88
	Foods consumed (n)	138	196	196	159	172
	Foods consumed by >3% of children(n)	48	52	53	56	52

Median serving sizes ranged from 1-307 grams/day (oil-buttermilk) for infants 6-8 months, 1-267 g/day for infants 9-11 months (oil-milk) and 1-234 g/day for children 12-23 months (oil-milk) and the actual types and amounts of foods consumed varied by region respectively. For example, milk servings in Tigray were much smaller than those of other regions; biscuits or sweet cookies were only consumed by >3% of children in the Oromia region. Although similar grains or legumes were consumed across all regions, the serving sizes varied by region. Fortified infant cereals were only included in the models in Tigray and Amhara regions because these food items were not consumed in the other regions. Eggs and starchy roots were not consumed in Amhara and Tigray regions respectively, while a starchy root like *enset* was only consumed in SNNPR and some parts of Oromia.

Problem nutrients

Zinc was a common problem nutrient in all regions and across all age groups. Iron was a problem nutrient for infants from 6-11 months of age in all regions but not for the oldest (12-23 months) age group (see **supplemental Table 2**). Calcium was a problem nutrient for the youngest age group in all regions, except SNNP region, for the 9-11 month age group in Tigray and Amhara regions and for the 12-23 month age group only in Amhara region. Niacin was a problem nutrient across the age groups in all regions except for the youngest age group (6-8 months of age) in Tigray and the oldest age group (12 to 23 months) in SNNP region. Thiamine, folate, vitamin A, vitamins B_{12} and B_6 were problem nutrients in some regions and age-groups, but not in all. The number of problem nutrients identified for children 12 to 23 months was greater than that of the younger age groups in Tigray and Amhara regions (see **supplemental Tables 3-14**).

Food Based Dietary Recommendations

A set of 24 alternative individual food-based recommendations, reflecting commonly consumed foods, were selected and tested in Module III (worst-case scenario analyses). A summary of the FBDRs selected for each region per age group is given in **Table 4**. These FBDRs do not include fruits because these foods were rarely consumed by the children and were not modelled (see **supplemental Table 1**).

FBDR combined with local complementary food products and supplementation

Table 5 shows the worst case scenario (Module III) of FBDR in combination with CF, MNP, Sq-LNS, or CF and MNP for 9-11 months old children in SNNPR. For example, we could add Sq-LNS to the FBDR 3.5 times per week (i.e., every other day) but its addition at a frequency of 7 times per week exceeded the energy constraints. Energy constraints also limited the addition of CF with Sq-LNS to the developed FBDR to just 2 servings/week. Similar results were found for the other regions and age groups (see **supplemental Table 3-Table 14**).

Table 4. Summary of food-based recommendations for different age groups per region in addition to breastmilk.

			6 to 8 mo.[1]	9 to 11 mo.[1]	12 to 23 mo.[1]
	Food group	*Foods[2]*	*s/wk.[3]*	*s/wk[3]*	*s/wk[3]*
Tigray	Dairy	Milk	7	7	7
	FICFP[4]		7	-	-
	Grains	Wheat, tef	4	7	14
	Vegetables	Vitamin C rich vegetables	-	7	3 to 4
	Legumes	Broad beans, vetch, (chick)peas	-	14	14
	Eggs		-	-	7
Amhara	Dairy	Milk	7	7	7
	FICFP		7	-	-
	Grains	Wheat, tef	-	14	14
	Vegetables[5]	Tomato, onions	-	-	14
	Legumes	Broad beans, lentils	7	7	21
	Starchy Roots	Potato	-	7	7
Oromia	Dairy	Milk	3 to 4	3 to 4	3 to 4
	Grains	Wheat, tef	7	14	14
	Vegetables[5]	Tomato, onion	-	14	14
	Legumes	Broad beans, lentils	7	3 to 4	14
	Starchy Roots	Potato	7	-	-
	Eggs		-	-	7
SNNPR	Dairy	(butter)milk	3 to 4	3 to 4	7
	Grains	Barley, millet, tef	14	35	21
	DGLV[6]	Kale	-	7	-
	Legumes	Chickpeas, kidney beans	21	14	21
	Starchy roots	Potato	-	3 to 4	-
	Eggs		-	-	7

[1] Months old; [2] Recommended foods within group; [3] Number of servings per week; [4] Fortified Infant Cereal Food Product; [5] Tomatoes and onion 14 servings; [6] Dark green leafy vegetables

There were regional differences in the ability of FBDR and MNP dosing regimens to ensure nutrient adequacy. For instance, FBDRs will likely ensure population-level nutrient adequacy for all nutrients except for zinc (all children), iron (6-11 months in all regions) and niacin (all 9-11 months, 6-8 months in Oromia and Tigray; and 12-23 months in Amhara). For children 9-11months in Tigray, Amhara and SNNP region; and 12-23 months in Amhara and Oromia; 1 serve of MNP per day would be required to reach nutrient adequacy whereas 1 serve per 2 days would be sufficient for 12-23 months in Tigray and SNNP region. However, the four groups that would not reach nutrient adequacy for all nutrients even when MNP was included on a daily basis are 6-8months in Tigray and Amhara; 6-8months and 9-11months in Oromia (**Figure 1**).

The prevalence of inadequate and excess intakes for iron and zinc are shown for the three age groups in **Table 6**. The prevalence of inadequate iron intakes at 10% bioavailability (between brackets at 5% bioavailability) was 77.7% (86.5%), 67.1% (81.6%) or 40.1% (52.9%) for 6-8, 9-11 or 12-23 months children, respectively, which was reduced to 39.8% (75.8%), 26.6% (66.5%), and 10.4% (35.5%), respectively, with simulated daily MNPs provision. Similarly, for zinc at moderate bioavailability (between brackets at low bioavailability), the prevalence of inadequate intakes were 92.7% (98.6%), 92.3% (100%), and 68.6 (96.1%)% for 6-8, 9-11 and 12-23 months old children respectively, which were all reduced to 0% when simulated with a daily MNPs provision, except for 12-23 months old children (53.9%) when using low zinc bioavailability. The prevalence of excess intakes was low, < 6.5%, for all nutrients for infants <12months, when the observed diet with or without provision of daily or every other day MNP were modelled using the WHO cut-off for UL. When using the IZiNCG cut-off for UL, prevalence of excess intake was 21.2% and 51.0% for 6-8 months old and 9-11 months old children, respectively. Prevalence of excess iron intake in children > 12 months of age was < 20% when only the observed diet was modelled. However, when simulating the provision of MNPs every other day or daily, the prevalence of excess intakes of iron was above 20% in 12-23 months old children, whereas the prevalence of excess intakes of zinc was also above 20% with daily, but not every other day MNPs supplementation, when the IZiNCG cut-off for UL was used. (See **Table 6**).

Discussion

The results of this study showed that for Ethiopian children 6-23 months of age, dietary improvements are possible using foods currently being consumed. However, even if FBDRs are fully implemented, our results suggest nutrient requirements still will not be met, for all children, for some nutrients ("problem nutrients"), in particular for zinc in all age groups, iron in 6-8 months old children, and niacin in 9-11 months old children. These results suggest that to ensure nutrient adequacy for all children in these populations the developed local FBDR should be combined with the provision of special fortified complementary foods or nutrient supplements.

Daily MNP supplementation, in addition to the FBDR, made it possible to meet nutrient needs for nearly all nutrients, however, calcium requirements were not met because the MNP contains no calcium. For children from 12 to 23 months, decreasing the frequency of MNPs consumption to one sachet every two days, in addition to FBDR, yielded a satisfactory nutrient content in all the 3 regions except Amhara where the zinc content of modelled diets remained low (53.9% of the RNI).

Adding Sq-LNS or a locally produced complementary food did not improve nutrient adequacy of the diet compared with FBDR alone. This result likely occurred because these nutrient-dense foods replaced other nutritious energy-delivering foods in the modelled diets, to avoid exceeding 100% of energy requirements in the model. We assume that in real life Sq-LNS interventions may still deliver substantial benefits to this population because (1) reported intake data from the NFCS suggested lower than recommended energy intakes for these age groups[10] and (2) we did not include cost constraints in the model and the best-modelled diets included some expensive food items. Sq-LNS may be a cheaper alternative food source for delivering additional energy and nutrients than the replaced food items. For instance, in two out of the four regions, fortified commercial infant cereals were reported to be consumed and were included in the model. When these fortified commercial infant cereals were not included in the model, the number of problem nutrients increased and only vitamin C, B_2 and vitamin A met the criteria for nutrient adequacy in Module III (testing FBDR) (data are not shown). These findings highlight the importance and confirm the need for cost-effective measures, such as fortification or home-fortification, to improve the nutrient adequacy, especially for the youngest age group. Future research should investigate whether food fortification, is a cost-effective strategy to increase dietary zinc intakes, to reduce the prevalence of zinc deficiency in this population[52].

We found that adding 3.5 or 7 servings per week of MNPs to the usual diets led to a decrease in the percentage of inadequate intakes for iron and zinc, without leading to a substantially increased risk of excessive intakes for iron. For zinc, daily MNP supplementation increased the risk of excess intakes to 51.0% of the population, which was reduced to <7% when the frequency of MNP use was reduced to every other day. These findings are in line with those observed in other studies confirming that in theory, the requirements of most, but not all, nutrients can be met by optimizing intakes of local foods[17, 53]. Interventions, such as MNPs can be used to further improve nutrient adequacy[54, 55]. However, concerns have been raised about possible side-effects of these interventions, including a possible, iron-induced increased morbidity from diarrhoea and other infectious diseases[56, 57]. In addition, in a recent study simulating the effects of home fortification of complementary foods in West Gojjam, Ethiopia, they observed a substantial increase in the risk of excessive intakes for iron and zinc in children 12-23 months of age[58]. These results are in contrast to our observations probably due to inter-study differences reflected in differences in the study population. There is uncertainty about tolerable upper intakes levels (UL), especially when bioavailability of iron and zinc are low in local diets[51, 59]. Therefore, some caution is warranted when interpreting these findings[28]. Even so, our findings suggest that, for the older age groups (12-23 months of age), using the more conservative IZiNCG upper limits, distribution of MNP on every other day may be a safer choice.

Table 5. Combinations of alternatives with nutrient values for 9-11months in SNNPR [1].

	%RNI													
	Protein	Fat	Calcium	Vit. C	Vit B-1	Vit B-2	Niacin	Vit. B-6	Folate	Vit. B-12	Vit. A	Iron*	Zinc**	N
FBDR‡	121.2	127.6	97.4	124.5	70.4	128	49	116.3	93	81.1	149.9	49.8	24.3	10
FBDR+ CF 3.5 s/wk.	143.6	129.9	98.7	128.6	87.5	134.3	57.6	131.1	118.6	81.1	150	54.8	27.9	10
FBDR+ MNP 3.5 s/wk.	121.2	127.6	97.4	174.5	153.8	190.5	124	199.6	186.8	145.4	149.9	65.9	48.7	11
FBDR+ MNP 7 s/wk.	121.2	127.6	97.4	224.5	237.1	253	199	283	280.5	209.6	149.9	82.1	73.1	13
FBDR+ Sq-LNS 1 s/wk.	124.8	133.5	107.4	138.8	84.6	142.2	63.3	130.3	107	91.2	164.2	54.4	37.9	9
FBDR+ Sq-LNS 3.5 s/wk.	134	148.5	132.4	174.5	120.2	177.7	99	165.7	142.7	116.6	199.9	65.9	71.9	12
FBDR+CF3.5 s/wk. +MNP 3.5 s/wk.	143.6	129.9	98.7	178.6	170.8	196.8	132.6	214.4	212.4	145.4	150	71	52.3	12
FDBR+CF3.5 s/wk. +MNP 7 s/wk.	143.6	129.9	98.7	228.6	254.2	259.3	207.6	297.8	306.1	209.7	150	87.1	76.6	13

[1] The minimized nutrient values (Module III) of different diet scenarios compared with % RNI for 9-11months in SNNPR using CF, MNP, Sq-LNS, and CF plus MNP; the combination highlighted with dotted line is the selected best combination; ‡ set of food based recommendations selected (see Table 4); *recommended nutrient intake for iron assuming 5% absorption; ** recommended nutrient intake for zinc assuming low absorption % RNI=% Recommended Nutrient Intake; N=Number of nutrient to reach at least 70% of the RNI in the worst case scenario; Vit=Vitamin; FBDR=Food Based Dietary Recommendations; CF=Local Complementary Food; s/wk=serving/week; MNP=Micronutrient Powder

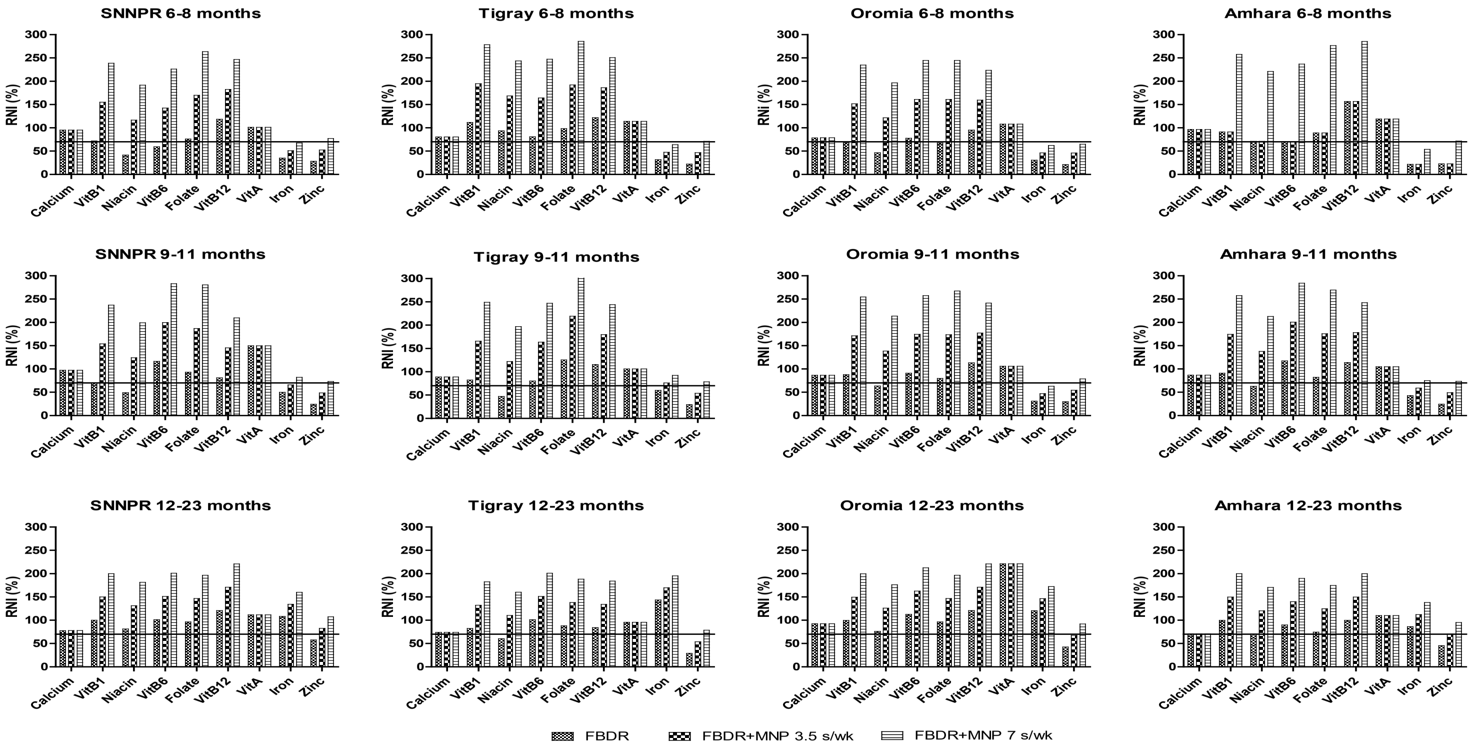

Figure 1. The minimized nutrient values (Module III) of different diet scenarios compared (% RNI) for 6-23 months old children in 4 regions in Ethiopia.

Table 6. Calculated inadequate and excess intakes (per age group) of selected nutrients at usual intake, addition of 1 MNP every other day (3.5 sachets/week) and daily.

Nutrient* (EAR)	Age group 6-8m (n=495) Inadequate %	Excess %	Age group 9-11m (n=465) Inadequate %	Excess %	Age group12-23m (n=1544) Inadequate %	Excess %
Iron(10%) **						
Usual diet	77.7	4.6	67.1	3.7	40.1	18.7
+1/2MNP/d	67.3	5.3	52.8	4.1	26.2	20.5
+1MNP/d	39.8	6.1	26.6	4.5	10.4	22.2
Iron(5%) **						
Usual diet	86.5	4.6	81.6	3.7	52.9	18.7
+1/2MNP/d	82.3	5.3	75.3	4.1	46.4	20.5
+1MNP/d	75.8	6.1	66.5	4.5	35.5	22.2
Zinc (moderate bioavailability) ∞ (WHO cut-off)						
Usual diet	92.7	0	92.3	0	68.6	0.1
+1/2MNP/d	0	0	0	0	8.2	0.1
+1MNP/d	0	0.2	0	0	0	0.1
Zinc (low bioavailability) ∞ (WHO cut-off)						
Usual diet	98.6	0	100	0	96.1	0.1
+1/2MNP/d	96.0	0	97.2	0	87.3	0.1
+1MNP/d	0	0.2	0	0	53.9	0.1
Zinc ≡ (IZiNCG cut-off)						
Usual diet		0.4		0		2.4
+1/2MNP/d		1.6		0.4		6.9
+1MNP/d		21.2		51.0		22.4

* Analysis was made using square root transformation for iron and log10 transformation for zinc and back transformed data to assess the inadequate and excess intake; **EAR for iron: Based on IOM (10%bioavailability) 6.9 mg/d and IOM (5% bioavailability) 13.8mg/d for 6-11months (p 324)[49]and based on WHO/FAO (10% of bioavailability) 5.8mg/d and WHO/FAO (5% bioavailability) 11.6mg/d for 12-23months were used (p 148); ∞EAR for Zinc (moderate bioavailability) 2.5mg/d and (low bioavailability) 5.0 mg/d for 6-11months based on IOM (p 466)[49] and 3.4mg/d (moderate bioavailability) and 6.9mg/d (low bioavailability)for 12-23months based on WHO/ FAO (p 148)[50] were used; UL: Upper Level for Iron based on IOM 40 mg for all target groups (p26-27)[49]. ∞ For zinc using WHO cut off 13mg for 6-11months, and 23 mg for 12- 23 months (p S120)[51]; ≡ using IZiNCG cut off 6mg for 6-11months, and 8mg for 12-23months (p S120)[51]; MNP/d: Micronutrient Powder/day

The results of our analysis confirm that dietary habits differ across the different geographical regions in Ethiopia due to differences in cultural practices between regions[60, 61]. For instance, eggs were not in the list of foods consumed by children from the Amhara region, most likely because animal source foods are not consumed during the long fasting season. In the other 3 regions, eggs could be recommended, at least for children 12-23 months of age. It is therefore advisable to develop separate food-based dietary recommendations for the different regions, taking into account differences across regions in food availability and consumption patterns. Regional differences in food intakes are known to exist in many countries.

In spite of the fact that the LP approach provides feasible and evidence-based results, this study has some limitations. First, in addition to the issue of the energy constraints described before, we calculated frequencies based on the percentage of the population who consumed each food because we did not have data on frequencies of food consumption. As the actual consumption frequency per food is more accurate than an estimated consumption using only one or two 24h recalls, using estimated consumption frequency may affect model input data and lead to bias in nutrient adequacy of some nutrients. The extent of this bias is, however, not known. Second, the feasibility of implementing regional FBDR should be assessed by household trials in order to identify barriers and supporting factors for the adoption of FBDRs. A translation of these theoretical FBDR into practical guidelines should take into account the feasibility of these guidelines, by field-testing the FBDR in practice. Furthermore, increasing access to nutritious foods that are part of a healthy diet, but currently not consumed frequently enough to feature in the models, continues to be necessary. Examples are fruits and vegetables, currently not included in the recommendations for the youngest children because they are not consumed frequently. Third, Optifood does not take into account all factors that affect food choices, such as variation in behaviour, food habits and the influence of social pressure on food choice. To some extent, the program takes this into account by using foods that are being consumed by at least 3% of the population. However, still, some of these foods may not be feasible options for part of the population, for example, fortified infant cereals which may be too costly. In general, it is known that the costs of diets based on nutritious local foods could be three to eight times higher than diets fortified with micronutrient powders (MNPs)[22] and costs were not included as a constraint in our analyses. Fourth, the intra-individual variation of the population was not quantifiable from survey data, to calculate the inadequate and excess intakes hence we used the variance from Uganda survey. However, the large number of survey days included provides a precise estimate of average intake at the population level which is advantageous for estimating median serving sizes[10, 28, 50].

Conclusion

Our results show that ensuring nutrient adequacy for a high percentage of 6-23- month-old Ethiopian children is difficult at least for some nutrients. Nutrient adequacy can be improved, in part, by promoting a diet with more vegetables (for >12 months children), legumes and animal source food that is currently consumed on average. However, the results suggest that even if the FBDRs are fully adopted, intakes of some nutrients, in particular, zinc, iron and perhaps niacin might remain suboptimal for some children in the population and additional interventions are required. The best nutritional option to reduce the nutrient gaps is a combination of the regional FBDRs with MNPs (6 mg iron/serving) supplementation; daily (for children < 12 months of age) and every other day (for children > 12 months of age). Our findings confirm that providing MNPs may potentially improve the nutrient adequacy of the diets of these children, while not leading to substantial excessive intakes. It is important to emphasize that MNP should not replace the feeding recommendations, but should be promoted in addition to these FBDRs together with breastfeeding on demand during the first two years of age. Our findings further suggest that region-specific FBDR are required, to account for differences between regions in food availability and dietary habits and to increase the acceptability of the recommendations. Hence, targeted approaches and dosing instructions have to be considered separately for children below 12 months of age and children above 12 months of age. The study also confirms the usefulness of LP analysis in order to explore and evaluate the effect of different options for nutrition interventions so as to inform policymakers.

List of abbreviations

CF: Complementary Food; EAR: Estimated Average Requirement; EHNRI: Ethiopian Health and Nutrition Research Institute; EPHI: Ethiopian Public Health Institute; FBDR: Food Based Dietary Recommendations; FAO: Food and Agriculture Organization; FCT: Food Composition Table; HAZ: Height-for-Age Z score; IOM: Institute of Medicine; IYCF: Infant and Young Child Feeding; IZiNCG: International Zinc Nutrition Consultative Group; LP: Linear Programming; MNP: Micronutrient Powder; NRC: National Research Council; NFCS: National Food Consumption Survey; RNI: Recommended Nutrient Intake; SD: Standard Deviation; SNNPR: South Nations, Nationalities and Peoples Region; Sq-LNS: Small quantity Lipid based Nutrient Supplement; UL: Tolerable Upper Intakes Level; UNICEF: United Nation Children's Fund; WAZ: Weight-for-Age Z score; WHZ: Weight-for-Height Z score; WHO: World Health Organization.

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Supplemental Tables

Supplemental Table 1. List of Foods consumed by >3% of children, median serving sizes (g/d) per age group, in Tigray, Amhara, Oromia, SNNP regions in Ethiopia

	Tigray			Amhara			Oromia			SNNPR		
	Age of children in months											
	6-8	9-11	12-23	6-8	9-11	12-23	6-8	9-11	12-23	6-8	9-11	12-23
Added fats												
Butter, spiced, clarified	-	-	-	-	-	-	6	8	2	3	3	5
Butter, un-spiced, raw	-	-	-	-	-	-	-	-	-	7	-	8
Oil, liquid	1	3	4	1	2	3	3	4	4	-	1	2
Shortening, fractionated, palm	3	5	3	-	2	3	4	6	4	-	4	3
Added sugars												
Sugar, refined	5	5	8	7	7	12	12	14	11	9	11	13
Bakery and breakfast cereals												
Biscuits, sweet cookies	-	-	-	-	-	-	18	16	-	-	-	-
Fortified infant cereal food	7	-	-	4	-	-	-	-	-	-	-	-
Dairy products												
Buttermilk, cow	-	-	-	-	-	-	-	-	-	307	154	173
Milk, cow, boiled	-	-	-	221	94	129	94	253	188	-	261	204
Milk, cow, fresh	52	137	126	134	162	129	218	267	234	148	113	173
Sour milk, cow	-	-	-	-	-	-	-	-	-	-	173	140
Fruits												
Avocado, fresh	-	-	-	-	-	-	-	-	-	-	-	74
Banana, fresh	-	-	-	-	-	-	-	-	-	-	-	105
Prickly pear	-	-	139	-	-	-	-	-	-	-	-	-
Grain and grain products												
Barley black, flour	-	-	16	1	3	3	14	16	5	1	3	3
Barley white, flour	9	13	26	2	9	6	9	18	10	-	16	5
Corn yellow, flour	-	-	5	-	-	2	3	2	5	-	3	4

Corn white, flour	-	4	14	-	24	13	5	21	47	-	21	39
Emmer wheat, flour	-	-	-	12	18	2	-	9	14	-	3	5
Macaroni, pasta dry	18	17	23	-	20	23	-	17	16	-	-	-
Millet black, flour	-	-	7	-	-	4	-	-	3	1	3	3
Millet mixed, flour	-	-	6	-	-	10	1	-	6	1	3	3
Millet white, flour	-	-	4	-	-	2	-	-	-	-	3	3
Rice, wholegrain	-	-	45	-	-	-	-	-	-	-	-	-
Sorghum red, flour	8	14	16	-	12	7	4	17	28	2	3	5
Sorghum mixed, flour	3	3	11	1	8	13	7	6	17	-	4	10
Sorghum white, flour	9	16	20	6	14	19	13	25	20	-	10	25
Tef red, flour	10	15	29	8	21	9	11	14	25	3	3	8
Tef mixed, flour	4	17	20	11	21	36	12	5	11	2	3	9
Tef white, flour	33	17	21	4	4	23	14	9	19	14	17	16
Wheat black, flour	5	20	69	-	-	10	4	-	3	-	3	3
Wheat mixed, flour	-	5	6	2	16	13	6	29	21	-	3	3
Wheat white, flour	15	31	39	14	10	21	12	29	40	1	8	25
Wheat wholegrain, flour	-	-	-	-	13	59	-	45	62	-	-	73
Legumes, nuts and seeds												
Broad beans, flour	1	-	4	3	2	6	-	9	8	1	3	3
Broad beans, split	-	-	7	-	-	16	-	-	9	-	-	-
Broad beans, whole fresh roasted	-	-	8	-	-	-	-	-	10	-	-	-
Chickpeas, flour	-	12	3	1	-	4	-	-	4	1	3	3
Kidney beans, whole, dried	-	-	-	-	-	2	-	-	-	1	3	8
Lentil, flour	-	-	-	1	-	2	-	-	-	1	3	3
Lentil, split	-	-	-	-	4	12	-	-	-	-	-	-
Lupine, raw	-	-	-	-	-	2	-	-	-	1	3	3
Partially ground grass pea	-	-	-	-	-	9	-	-	-	-	-	-
Peas, flour	4	4	6	2	-	5	2	5	7	1	2	4
Peas, split	-	-	14	-	-	20	-	-	-	-	-	-
Peas whole, fresh, roasted	3	12	10	-	-	-	-	15	11	-	-	-
Vetch, flour	1	4	7	7	6	9	-	4	7	1	3	4
Meat, fish and eggs												
Egg whole, raw	-	35	16	-	16	-	28	43	43	-	22	25

Chapter 3

Starchy roots and plants												
False banana, flour	-	-	-	-	-	-	-	-	-	-	39	48
False banana, kocho	-	-	-	-	-	-	-	-	69	-	70	55
Potato Irish, boiled	-	-	-	-	-	40	-	-	142	-	106	120
Potato Irish, raw	-	-	-	-	38	32	13	41	48	-	79	43
Taro, boiled	-	-	-	-	-	-	-	-	-	-	-	104
Vegetables												
Chili, boiled	-	-	-	-	1	2	-	-	-	-	-	-
Ethiopian kale, raw	-	-	-	-	-	-	-	-	45	-	29	27
Green pepper, raw	-	-	1	-	-	7	-	4	6	-	11	4
Onion bulb, raw or boiled	-	2	8	-	-	9	-	9	12	-	-	-
Onion shallot, raw	4	6	7	10	4	15	13	12	9	-	4	5
leek, raw	-	-	-	-	8	-	-	-	-	-	-	4
Tomato, raw	8	7	12	-	6	18	-	18	15	-	-	-

Supplemental Table 2. Summary of problem nutrients that can be solved with FBDR and those persisting after FBDR, by age group for each region

		Calcium	Thiamin	Niacin	Vit. B-6	Folate	Vit. B-12	Vit. A	Iron	Zinc
Tigray	6 to 8 mo.	Yellow							Red	Red
	9 to 11 mo.	Yellow		Red					Red	Red
	12 to 23 mo.			Yellow		Yellow				Red
Amhara	6 to 8 mo.	Yellow		Yellow	Yellow	Yellow			Red	Red
	9 to 11 mo.	Yellow		Red					Red	Red
	12 to 23 mo.	Yellow		Red		Yellow	Yellow	Yellow		Red
Oromia	6 to 8 mo.	Yellow	Red	Red		Red			Red	Red
	9 to 11 mo.			Red					Red	Red
	12 to 23 mo.			Yellow						Red
SNNP	6 to 8 mo.		Yellow	Red	Red	Yellow			Red	Red
	9 to 11 mo.			Red					Red	Red
	12 to 23 mo.									Red

Yellow: Nutrient requirements that can be met require changes consistent with FBDR

Red: Nutrient requirements cannot be met by any combination of local foods

Problem nutrients are nutrients for which it may be difficult to ensure nutrient adequacy with local foods alone (when the maximized RNI is <100%).

Partial problem nutrients are nutrients when the minimized %RNI <70% and the maximized RNI ≥ 100%

Supplemental Table 3-Table 14

Supplemental Table 3. The optimal[1], best-case scenario[2] and worst-case scenario[3] of the baseline diet, the worst-case scenario for the food based recommendations and each alternative combination expressed as a percentage of the recommended nutrient intake in 6 to 8 mo. infants of Tigray region

	Protein	Fat	Calcium	Vit. C	Vit B-1	Vit. B-2	Niacin	Vit. B-6	Folate	Vit. B-12	Vit. A	Iron4	Zinc5	N6
Baseline diet7	129.7	160.5	82.4	124.5	126.1	147.7	104.1	100	111.6	122.1	114.6	37.1	24.1	11
best-case scenario8	137.4	169.8	82.7	125.1	127.5	148.6	106.3	101.3	112.8	122.2	114.9	37.4	25.1	11
worst-case scenario	107.2	145.4	54.4	109.9	44.4	66.1	39.2	40.9	48.7	47.6	100.5	5.4	17.4	4
FBDR9	115.1	159.5	80.7	113.7	111.7	140.9	93.7	80.8	98.4	121.9	114	31.5	22.4	11
CF 3.5 s/wk.10	114.7	145.2	56	110.2	56.3	71.8	48.1	52.2	78.2	47.6	100.5	14.6	18.1	6
CF 7 s/wk.	134.7	145.8	58.5	110.5	74.8	80.6	61.8	69.7	110.6	47.7	100.6	26.7	21.1	7
MNP 3.5 s/wk.	107.2	145.4	54.4	159.9	127.7	128.6	114.2	124.2	142.5	111.9	100.5	21.5	41.8	10
MNP 7 s/wk.	107.2	145.4	54.4	209.9	211.1	191.1	189.2	207.6	236.2	176.2	100.5	37.6	66.2	10
sq-LNS 3.5 s/wk.	101.6	167.4	88.3	159.8	85.2	111.6	82.6	80.9	94.2	83.1	150.5	18.2	62.4	11
sq-LNS 7 s/wk.	104.3	189.9	122.7	209.8	130.9	159.4	129.2	124.3	141.2	118.6	200.5	33.3	108.6	12
FBDR+ CF 2 s/wk.	129.6	159.9	82.3	113.9	122.9	146.3	102.2	91.9	117.5	121.9	114	38.6	24.4	11
FBDR+MNP 3.5 s/wk.	115.1	159.5	80.7	163.7	194.9	203.4	168.7	164.1	192.2	186.2	114	47.7	46.8	11
FBDR+ MNP 7 s/wk.	115.1	159.5	80.7	213.7	278.3	265.9	243.7	247.4	285.9	250.5	114	63.8	71.2	12
FBDR+ sq-LNS 2 s/wk.	97.4	120.9	172.5	100.6	142.3	138.9	121.4	107.5	126.3	142.2	142.5	40.5	49.4	11
FBDR+CF2 s/wk.+ MNP 3.5 s/wk.	129.6	159.9	82.3	163.9	206.2	208.8	177.2	175.3	211.3	186.2	114	54.7	48.8	11
FBDR+CF 2 s/wk. +MNP 7 s/wk.11	129.6	159.9	82.3	213.9	289.5	271.3	252.2	258.6	305	250.5	114	70.9	73.2	13
FBDR+ CF1 s/wk. + sq-LNS 1 s/wk.	125.2	166.2	91.5	128.1	130.9	157.6	111.8	99.7	121.9	132.1	128.3	39.6	36.9	11

[1] The optimal diet formulated by using goal programming (Optifood module II)
[2] Each diet sequentially maximizes each micronutrient (Optifood module III)
[3] Each diet sequentially minimizes each micronutrient (Optifood module III)
[4] Recommended nutrient intake for iron assuming 5% absorption
[5] Recommended nutrient intake for zinc assuming low absorption.
[6] Number of nutrients to cover at least 70% of the recommended nutrient intake in the worst-case scenario.
[7] Nutritionally best possible diet (Optifood module II).
[8] Diet sequentially maximizes each nutrient (Optifood module III).
[9] Set of food based dietary recommendations selected.
[10] s/wk.=number of servings per week.
[11] Best alternative option

Supplemental Table 4. The optimal[1], best-case scenario[2] and worst-case scenario[3] of the baseline diet, the worst-case scenario for the food based recommendation and alternative combinations expressed as a percentage of the recommended nutrient intake in 9 to 11 mo. infants of Tigray region.

	Protein	Fat	Calcium	Vit C	Vit B-1	Vit B-2	Niacin	Vit B-6	Folate	Vit B-12	Vit A	Iron[4]	Zinc[5]	N[6]
Baseline diet [7]	177.3	153.5	75.9	121.8	100	134.5	57.6	105	148.6	122	132.7	71.9	33.2	11
best-case scenario[8]	194.3	187.9	92.9	130.1	108.5	174.9	71.1	119.1	157	164.6	139.6	74.1	35.7	12
worst-case scenario	112.5	124.3	52.3	102.5	59.8	68.3	38.9	55.4	53	44.8	93.8	11.3	18.6	4
FBDR[9]	153.6	156.1	88.9	127.5	82.3	145.8	47.2	80.4	125.6	115.6	106.2	60	29.5	10
CF 3.5 s/wk.[10]	118.1	123.6	53.5	102.9	67	72.4	50.5	64.2	81.7	44.8	93.8	19	19.2	6
CF 7 s/wk.	126.8	123.7	55.3	103.2	77.3	79	62.4	75.1	110.8	44.8	93.9	27.6	21.1	8
MNP 3.5 s/wk.	112.5	124.3	52.3	152.5	143.1	130.8	113.9	138.7	146.8	109.1	93.8	27.5	43.1	10
MNP 7 s/wk.	112.5	124.3	52.3	202.5	226.5	193.3	188.9	222	240.5	173.4	93.8	43.6	67.5	10
sq-LNS 3.5 s/wk.	104.9	143.8	85.9	152.5	97.1	112.6	84.9	93.6	98	80.3	143.8	23.1	63.5	11
sq-LNS 7 s/wk.	104.9	163.5	119.9	202.5	136.4	158.7	131.1	132.7	143	115.8	193.8	35.2	109.1	12
FBDR+ CF 1 s/wk.	161.2	156.3	89.7	127.6	88.5	148.8	51.9	86.8	135.5	115.6	106.2	63.7	30.6	10
FBDR+MNP 3.5 s/wk.	153.6	156.1	88.9	177.5	165.7	208.3	122.2	163.7	219.4	179.9	106.2	76.2	53.9	12
FBDR+ MNP7 s/wk.	153.6	156.1	88.9	227.5	249	270.8	197.2	247	313.1	244.2	106.2	92.3	78.3	13
FBDR+ MNP 6 s/wk.[11]	153.6	156.1	88.9	213.2	225.2	252.9	175.8	223.2	286.3	225.8	106.2	87.7	71.4	13
FBDR+ sq-LNS 1 s/wk.	157.3	162	98.9	141.8	96.6	160	61.5	94.6	139.9	125.8	120.5	64.7	43.1	10
FBDR+ CF1 s/wk. + MNP3.5 s/wk.	188.2	170.2	89.4	170.8	167.9	225.6	121.4	171.1	241.9	228.6	139.1	75.1	54.5	12
FBDR+ CF1 s/wk. + MNP 7 s/wk.	188.2	170.2	89.4	220.8	251.2	288.1	196.4	254.4	335.7	292.9	139.1	91.2	78.9	13
FBDR+ CF 1 s/wk. + MNP 6 s/wk.	188.2	170.2	89.4	206.5	227.4	270.3	175	230.6	308.9	274.5	139.1	86.6	71.9	13
FBDR+ CF+ sq-LNS	NP[12]	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP

[1] The optimal diet formulated by using goal programming (Optifood module II)
[2] Each diet sequentially maximizes each micronutrient (Optifood module III)
[3] Each diet sequentially minimizes each micronutrient (Optifood module III)
[4] Recommended intake for iron assuming 5% absorption.
[5] Recommended intake for zinc assuming low absorption.
[6] Number of nutrients that cover at least 70% of the recommended nutrient intake in the worst case scenario.
[7] Nutritionally best possible diet (Optifood module II)
[8] Diet sequentially maximizes each nutrient (Optifood module III).
[9] Set of food based dietary recommendations selected.
[10] s/wk.=number of servings per week.
[11] Best alternative option
[12] NP= Combination not possible due to energy constraints

Supplemental Table 5. The optimal[1], best-case scenario[2] and worst-case scenario[3] of the baseline diet; the worst-case scenario for the food based recommendations and alternative combinations expressed as a percentage of the recommended nutrient intake in 12 to 23 mo. infants of Tigray region.

	Protein	Fat	Calcium	Vit C	Vit B-1	Vit B-2	Niacin	Vit B-6	Folate	Vit B-12	Vit A	Iron[4]	Zinc[5]	N[6]
Baseline diet[7]	212.3	121.6	100	177.6	95.7	146.4	59.4	108	81.7	100	111.2	100	64.8	11
best-case scenario[8]	223.2	137.8	109.9	193.9	117.3	161.4	86.1	127.7	87.1	101.4	111.8	144.3	70.4	13
worst-case scenario	143.4	90.5	40.9	91.4	59.5	61.1	37.1	65.8	35.7	31.9	83.6	39.9	24.4	4
FBDR[9]	213.4	119.5	70.6	114.8	99.8	140	70.4	89.8	74.5	99.9	110.2	86.3	45.7	12
CF 3.5 s/wk.[10]	152.1	89.5	41.6	91.9	62.1	66	45.2	67.65	57.45	31.9	83.7	57.25	24.25	4
CF 7 s/wk.	165.1	89.7	43.4	92.4	68.5	72.4	55.7	72	80.4	31.9	83.7	76.7	26.7	8
MNP 3.5 s/wk.	143.4	90.5	40.9	141.4	109.5	111.1	87.1	115.8	85.7	81.9	83.6	65.7	49.1	10
MNP 7 s/wk.	143.4	90.5	40.9	191.4	159.5	161.1	137.1	165.8	135.7	131.9	83.6	91.6	73.8	12
sq-LNS 3.5 s/wk.	136.1	105.6	67.3	141.4	79.6	96.1	65.7	85.1	58.5	59.4	133.6	57.7	69.1	7
sq-LNS 7 s/wk.	136.1	120.8	93.8	191.4	100.3	132.5	94.6	105	82.5	87	183.6	76.7	114.2	13
FBDR+ CF	NP[11]	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0
FBDR+ MNP 3.5 s/wk.[12]	213.4	119.5	70.6	164.8	149.8	190	120.4	139.8	124.5	149.9	110.2	112.1	70.4	13
FBDR+ MNP 7 s/wk.	213.4	119.5	70.6	214.8	199.8	240	170.4	189.8	174.5	199.9	110.2	138	95.1	13
FBDR+ sq-LNS 1 s/wk.	216.8	124.2	78.6	129.1	108.3	151.4	79.9	98.3	82.1	107.8	124.5	93.7	59.4	12
FBDR+CF +MNP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0
FBDR+ CF+ sq-LNS	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0

1 The optimal diet formulated by using goal programming (Optifood module II)
2 Each diet sequentially maximizes each micronutrient (Optifood module III)
3 Each diet sequentially minimizes each micronutrient (Optifood module III)
4 Recommended nutrient intake for iron assuming 5% absorption.
5 Recommended nutrient intake for zinc assuming low absorption.
6 Number of nutrients that cover at least 70% of the recommended nutrient intake in the worst-case scenario
7 Nutritionally best possible diet (Optifood module II)
8 Diet sequentially maximizes each nutrient (Optifood module III).
9 Set of food based dietary recommendations selected.
10 s/wk.=number of servings per week
11 NP= Combination not possible due to energy constraints
12 Best alternative option

Supplemental Table 6. The optimal,[1] best-case scenario[2] and worst-case scenario[3] of the baseline diet; the worst-case scenario for the food based recommendations and alternative combinations expressed as a percentage of the recommended nutrient intake in 6 to 8 mo. infants of Amhara region.

	Protein	Fat	Calcium	Vit. C	Vit B-1	Vit B-2	Niacin	Vit. B-6	Folate	Vit. B-12	Vit. A	Iron[4]	Zinc[5]	N[6]
Baseline[7]	133.3	159.8	78	116.6	102.1	130.6	81	91.9	99.1	103.6	110.4	34	21.4	11
best-case scenario[8]	150.4	189.7	97.8	123.6	103.8	173.9	81.5	93.2	99.2	157	119.2	34.6	24.1	11
worst-case scenario	110.1	147.4	61.3	111.1	51.5	82.5	36.7	45.4	50.8	55.1	101.8	9.1	17.2	5
FBDR[9]	148	184.3	96.7	121	91.3	172.3	71.1	70.2	89	156.7	118.9	21.6	22.8	11
CF 3.5 s/wk.[10]	114.1	144.9	55.5	110.8	58.3	72.6	46.6	52.5	77.2	47.6	100.6	12.3	18	6
CF 7 s/wk.	133	145.8	57	111.7	70.3	78.1	58.7	65.5	106.2	47.7	100.6	17.8	21.7	7
MNP 3.5 s/wk.	110.1	147.4	61.3	161.1	134.8	145	111.7	128.8	144.6	119.4	101.8	25.5	41.6	10
MNP 7 s/wk.	110.1	147.4	61.3	211.1	218.1	207.5	186.7	212.1	238.3	183.7	101.8	41.4	66	10
sq-LNS 3.5 s/wk.	102.1	166.8	88.6	159.9	90.8	115.7	82.7	84.2	95.8	83.1	150.5	20.9	61.7	11
sq-LNS 7 s/wk.	103.9	188.9	122.7	209.8	131	159.5	129.2	124.4	141.2	118.6	200.5	33.3	108.6	12
FBDR+ CF	NP[11]	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0
FBDR+ MNP 3.5 s/wk.	148	184.3	96.7	121	91.3	172.3	71.1	70.2	89	156.7	118.9	21.6	22.8	11
FBDR+ MNP 7 s/wk.[12]	148	184.3	96.7	221	257.9	297.3	221.1	236.9	276.5	285.3	118.9	53.8	71.6	12
FBDR+ sq-LNS	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0
FBDR+CF +MNP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0
FBDR+ CF+ sq-LNS	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0

1 The optimal diet formulated by using goal programming (Optifood module II)
2 Each diet sequentially maximizes each micronutrient (Optifood module III)
3 Each diet sequentially maximizes each micronutrient (Optifood module III)
4 Recommended nutrient intake for iron assuming 5% absorption
5 Recommended nutrient intake for zinc assuming low absorption
6 Number of nutrients to cover at least 70% of the recommended nutrient intake in the worst-case scenario.
7 Nutritionally best possible diet (Optifood module II)
8 Diet sequentially maximizes each nutrient (Optifood module III).
9 Set of food based dietary recommendations selected
10 s/wk.=number of servings per week
11 NP= Combination not possible due to energy constraints
12 Best alternative option

Supplemental Table 7. The optimal[1], best-case scenario[2] and worst-case scenario[3] of the baseline diet; the worst-case scenario for the food based recommendations and alternative combinations expressed as a percentage of the recommended nutrient intake for 9 to 11 mo. infants of Amhara region.

	Protein	Fat	Calcium	Vit. C	Vit B-1	Vit B-2	Niacin	Vit. B-6	Folate	Vit. B-12	Vit. A	Iron[4]	Zinc[5]	N[6]
Baseline[7]	152.4	145.3	74.4	130.1	98.4	132.6	68.4	128.6	100	100	114.8	51.7	26.9	10
best-case scenario[8]	179	171.6	90.2	138.5	107.8	164.4	76.5	140.2	108.3	136.4	120.9	54.5	32.9	11
worst-case scenario	104.1	122.9	51.6	102.5	59.7	68.3	42	55.4	53	44.8	93.8	11.3	18.3	4
FBDR[9]	144.6	153.6	86.8	129.3	91.1	153.4	62.9	117.3	82	113.8	104.8	42.8	24.7	10
CF 3.5 s/wk.[10]	115.5	123.3	53	103.7	66.7	72.1	52.8	64.2	86.1	44.9	93.9	15.2	19.7	6
CF 7 s/wk.	131.4	124	54.7	104.9	80.4	80	65.3	77.5	120.7	44.9	93.9	22.3	22.9	8
MNP 3.5 s/wk.	104.1	122.9	51.6	152.5	143	130.8	117	138.7	146.7	109.1	93.8	27.4	42.7	10
MNP 7 s/wk.	104.1	122.9	51.6	202.5	226.4	193.3	192	222.1	240.5	173.4	93.8	43.5	67.1	10
sq-LNS 3.5 s/wk.	102.4	142.7	85.7	152.5	97.4	112	86.4	94.2	98	80.3	143.8	23.1	63.2	11
sq-LNS 7 s/wk.	102.4	162.8	119.9	202.5	136.7	159.1	132.4	133.6	143.1	115.8	193.8	35.2	108.8	12
FBDR+ CF	NP[11]	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0
FBDR+ MNP 3.5 s/wk.	144.6	153.6	86.8	179.3	174.4	215.9	137.9	200.7	175.7	178.1	104.8	59	49.1	11
FBDR+ MNP 7 s/wk.[12]	144.6	153.6	86.8	229.3	257.7	278.4	212.9	284	269.5	242.4	104.8	75.1	73.5	13
FBDR+ sq-LNS	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0
FBDR+CF +MNP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0
FBDR+ CF+ sq-LNS	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0

1 The optimal diet formulated by using goal programming (Optifood module II).
2 Each diet sequentially maximizes each micronutrient (Optifood module III).
3 Each diet sequentially minimizes each micronutrient (Optifood module III).
4 Recommended nutrient intake for iron assuming a 5% absorption
5 Recommended nutrient intake for zinc assuming low absorption
6 Number of nutrient to cover at least 70% of the recommended nutrient intake in the worst-case scenario.
7 Nutritionally best possible diet (Optifood module II)
8 Diet sequentially maximizes each nutrient (Optifood module III).
9 Set of food based dietary recommendation selected
10 s/wk=number of Servings per week
11 NP= Combination not possible due to energy constraints
12 Best alternative option

Supplemental Table 8. The optimal[1], best-case scenario[2] and worst-case scenario[3] of the baseline diet; the worst-case scenario for the food based recommendations and alternative combinations expressed as a percentage of the recommended nutrient intake for 12 to 23 mo. children from Amhara region.

	Protein	Fat	Calcium	Vit. C	Vit B-1	Vit B-2	Niacin	Vit. B-6	Folate	Vit. B-12	Vit. A	Iron[4]	Zinc[5]	N[6]
Baseline[7]	214.5	117.2	77.7	135.3	98.5	145.6	67.8	111.5	99.1	84.2	95.6	168.1	37.1	11
best-case scenario[8]	224.4	130.7	78.4	141.2	106.1	148.9	71.8	125.5	99.8	84.3	95.7	173.9	42.4	12
worst-case scenario	151.9	91.1	45.8	94.3	65.1	72.9	41.6	64.6	40.3	31.9	83.6	45.7	24.1	5
FBDR[9]	192.6	113.7	74.1	134.2	82.3	136.9	60.4	101	88.1	84.2	95.5	143.7	29.2	11
CF 3.5 s/wk.[10]	147.5	90.2	41.7	93.1	63.2	68.1	47.4	62.5	56.4	31.9	83.7	48.3	24.2	4
CF 7 s/wk.	159.2	90.3	41.9	94.3	65.6	69.6	54.2	66.3	77.5	31.9	83.8	54.9	26.1	6
MNP 3.5 s/wk.	151.9	91.1	45.8	144.3	115.1	122.9	92.6	114.6	90.3	81.9	83.6	71.6	48.8	11
MNP 7 s/wk.	151.9	91.1	45.8	194.3	165.1	172.9	141.6	164.6	140.3	131.9	83.6	97.4	73.5	12
sq-LNS 3.5 s/wk.	132.1	106	69.1	142.7	83.7	104.2	70	83.2	60.4	59.4	133.6	61	68.8	8
sq-LNS 7 s/wk.	132.1	121.2	95	191.6	103.7	136	98.4	102.2	83.2	87	183.6	78.3	113.7	13
FBDR+ CF 2 s/wk.	213.4	114.6	75.5	135	92.2	143.1	68.8	111.4	103	84.2	95.5	155.2	32.8	11
FBDR+ MNP 3.5 s/wk.	192.6	113.7	74.1	184.2	132.3	186.9	110.4	151	138.1	134.2	95.5	169.6	53.9	12
FBDR+MNP 7 s/wk.	192.6	113.7	74.1	234.2	182.3	236.9	160.4	201	188.1	184.2	95.5	195.4	78.6	13
FBDR+ MNP 6 s/wk.	192.6	113.7	74.1	219.9	168	222.6	146.1	186.7	173.8	169.9	95.5	188	71.5	13
FBDR+ sq-LNS 3 s/wk.[11]	202.9	127.7	98.1	177.1	107.8	171	88.9	126.5	111	107.8	138.3	165.9	70.5	13
FBDR+CF 2 s/wk. +MNP 3.5 s/wk.	213.4	114.6	75.5	185	142.2	193.1	118.8	161.4	153	134.2	95.5	181.1	57.5	12
FBDR+CF 2 s/wk. +MNP 7 s/wk.	213.4	114.6	75.5	235	192.2	243.1	168.8	211.4	203	184.2	95.5	206.9	82.2	13
FBDR+CF 2 s/wk. +MNP 6 s/wk.	213.4	114.6	75.5	220.7	177.9	228.8	154.5	197.1	188.7	169.9	95.5	199.5	75.1	13
FBDR+ CF1 s/wk. + sq-LNS 2	209.9	123.5	90.8	163.2	104.3	162.7	83.6	123.2	110.8	100	124.1	164.2	58.6	13

[1] The optimal diet formulated by using goal programming (Optifood module II).
[2] Each diet sequentially maximizes each micronutrient (Optifood module III)
[3] Each diet sequentially minimizes each micronutrient (Optifood module III)
[4] Recommended nutrient intake for iron assuming 5% absorption
[5] Recommended nutrient intake for zinc assuming low absorption
[6] Number of nutrients to cover at least 70% of the recommended nutrient intake of the worst-case scenario.
[7] Nutritionally best possible diet (Optifood module II)
[8] Diet sequentially maximizes each nutrient (Optifood module III).
[9] Set of food based dietary recommendations selected
[10] s/wk=number of servings per week
[11] Best alternative option

Supplemental Table 9. The optimal[1], best-case[2] and worst-case scenario[3] of the baseline diet; the worst-case scenario for the food based recommendations and alternative combinations expressed as a percentage of the recommended nutrient intake in children from 6 to 8 mo. of Oromia region.

	Protein	Fat	Calcium	Vit. C	Vit B-1	Vit B-2	Niacin	Vit. B-6	Folate	Vit. B-12	Vit. A	Iron[4]	Zinc[5]	N[6]
Baseline[7]	144.6	164.3	69.1	125.3	74.5	105.8	45.9	100	90.2	100	129.3	38.4	23.3	9
best-case scenario[8]	168	205.3	97.8	134.3	81	165.5	61	109.2	94.3	161.5	139.3	45.2	28.8	10
worst-case scenario	83.8	143.7	53.2	109.9	34.9	62.1	31.6	29.3	44.3	47.6	100.5	2.3	13.8	4
FBDR[9]	130	167.3	78.4	126.8	67.9	118.3	46.5	77.7	67.3	95	108.1	30.5	21.2	8
CF3.5 s/wk.[10]	98.9	144.6	54.7	111.6	51.2	65.5	36.6	42.3	68	47.6	100.6	12.6	16.2	4
CF 7 s/wk.	122.6	147.1	56.6	113.3	71.3	71.3	44	59.8	94.8	47.6	100.7	24.2	19.2	7
MNP 3.5 s/wk.	83.8	143.7	53.2	159.9	118.3	124.6	106.6	112.7	138.1	111.9	100.5	18.5	38.2	10
MNP 7 s/wk.	83.8	143.7	53.2	209.9	201.6	187.1	181.6	196	231.8	176.2	100.5	34.6	62.6	10
sq-LNS 3.5 s/wk.	89.6	165.7	87.8	159.8	81.1	109.6	79.2	74.6	91.4	83.1	150.5	17.2	61	11
sq-LNS 7 s/wk.	103.9	188.8	122.7	209.8	130.8	159.4	129.2	124.2	141.2	118.6	200.5	33.3	108.6	12
FBDR+ CF	NP[11]	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0
FBDR+ MNP 3.5 s/wk.	130.2	167.3	78.5	176.8	151.6	180.5	121.6	161.2	161.2	159.3	108.1	46.3	46.1	11
FBDR+ MNP 7 s/wk.[12]	130.2	167.3	78.5	226.8	234.9	243	196.6	244.5	254.9	223.5	108.1	62.4	64.8	11
FBDR+ sq-LNS	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0
FBDR+CF +MNP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0
FBDR+ CF+ sq-LNS	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0

1 The optimal diet formulated by using goal programming (Optifood module II).
2 Each diet sequentially maximizes each micronutrient (Optifood module III).
3 Each diet sequentially minimizes each micronutrient (Optifood module III).
4 Recommended nutrient for iron intake assuming 5% absorption
5 recommended nutrient intake for zinc assuming low absorption
6 Number of nutrient to cover at least 70% of the recommended nutrient intake in the worst-case scenario.
7 Nutritionally best possible diet (Optifood module II)
8 Diet sequentially maximizes each nutrient (Optifood module III).
9 Set of food based dietary recommendations selected
10 s/wk=number of servings per week
11 NP= Combination not possible due to energy constraints
12 Best alternative option

Supplemental Table 10. The optimal[1], best-case scenario[2] and worst-case scenario[3] of the baseline diet; the worst-case scenario for the food based recommendations and alternative combinations expressed as a percentage of the recommended nutrient intake for infants of 9 to 11 mo. in Oromia region.

	Protein	Fat	Calcium	Vit. C	Vit B-1	Vit B-2	Niacin	Vit. B-6	Folate	Vit. B-12	Vit. A	Iron[4]	Zinc[5]	N[6]
Baseline[7]	181.8	161	80.3	133.3	100	155.1	65.8	111.6	105.8	146.2	142.8	44.8	35.2	10
best-case scenario[8]	202	218	113.7	167.7	114.2	221.5	99.5	166.8	133.6	232.7	155.8	51	37.9	11
worst-case scenario	75.8	122	49.9	102.5	36.2	59.6	31.6	33.9	43.6	44.8	93.8	2.8	14.2	4
FBDR[9]	148.2	154	86.5	131.3	87.9	147.6	63.5	91	79.8	113	105.8	31	29.9	10
CF3.5 s/wk.[10]	86.2	123	51.3	104.2	50.5	62.4	35.2	42.5	66	44.8	93.9	12.8	15.4	4
CF 7 s/wk.	105.8	124	53.1	105.9	69.4	67.5	42	58.5	92.1	44.8	94	24.1	18.2	5
MNP 3.5 s/wk.	75.8	122	49.9	152.5	119.5	122.1	106.6	117.3	137.3	109.1	93.8	18.9	38.6	10
MNP 7 s/wk.	75.8	122	49.9	202.5	202.9	184.6	181.6	200.6	231.1	173.4	93.8	35.1	63	10
sq-LNS 3.5 s/wk.	79.6	142	84.4	152.5	81.4	107	78.5	76.4	89.9	80.3	143.8	17.6	60.4	11
sq-LNS 7 s/wk.	89	162	119.3	202.5	129.1	155.7	127.3	123	138.6	115.8	193.8	33.3	107.7	12
FBDR+ CF 1 s/wk.	154.3	154	87	131.8	93.7	149.3	65.6	96.1	87.4	113	105.8	34.3	30.7	10
FBDR+ MNP 3.5 s/wk.	148.2	153	86.5	181.3	171.2	210.1	138.5	174.3	173.5	177.3	105.8	47.1	54.3	11
FBDR+ MNP 7 s/wk.	148.2	153	86.5	231.3	254.5	272.6	213.5	257.7	267.3	241.6	105.8	63.2	78.7	12
FBDR+ sq-LNS 1 s/wk.	151.9	159	96.5	145.6	102.2	161.8	77.7	105.3	94.1	123.3	120	35.6	43.5	11
FBDR+CF1 s/wk. +MNP 3.5 s/wk.	154.3	154	87	181.8	177	211.8	140.6	179.4	181.2	177.3	105.8	50.4	55.1	11
FBDR+CF 1 s/wk. +MNP 7 s/wk.[11]	154.3	154	87	231.8	260.3	274.3	215.6	262.7	274.9	241.6	105.8	66.5	79.5	12
FBDR+ CF+ sq-LNS	NP[12]	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0

[1] The optimal diet formulated by using goal programming (Optifood module II).
[2] Each diet sequentially maximizes each micronutrient (Optifood module III).
[3] Each diet sequentially minimizes each micronutrient (Optifood module III).
[4] Recommended nutrient intake for iron assuming 5% absorption
[5] Recommended nutrient intake for zinc assuming low absorption
[6] Number of nutrient to cover at least 70% of the recommended nutrient intake in the worst-case scenario.
[7] Nutritionally best possible diet (Optifood module II)
[8] Diet sequentially maximizes each nutrient (Optifood module III).
[9] Set of food based dietary recommendations selected
[10] s/wk=number of servings per week
[11] Best alternative option
[12] NP= Combination not possible due to energy constraints

Supplemental Table 11. The optimal[1], best-case scenario[2] and worst-case scenario[3] of the baseline diet; the worst-case scenario for the food based recommendations and alternative combinations expressed as a percentage of the recommended nutrient intake in 12 to 23 mo. children of Oromia region.

	Protein	Fat	Calcium	Vit. C	Vit B-1	Vit B-2	Niacin	Vit. B-6	Folate	Vit. B-12	Vit. A	Iron[4]	Zinc[5]	N[6]
Baseline[7]	248.5	130.5	100	159.8	103.4	185.5	75.1	120	100	131.4	223.4	134.9	46.9	12
best-case scenario[8]	265.2	170.3	118.3	192	115.5	225.8	95.5	162.8	104.5	171.4	231.5	162.3	53.4	12
worst-case scenario	120.7	90.7	38.8	91.4	56.5	58.2	32.7	59.7	34.3	31.8	83.6	42.4	22.2	3
FBDR[9]	239.3	125.4	92.6	152	99.6	174.2	76.1	112.6	96.7	120.8	221.1	120.5	42.6	12
CF3.5 s/wk.[10]	126	90.8	39.6	94	58	57	34.3	56.5	50.7	31.8	83.7	55	21.3	4
CF 7 s/wk.	132.7	91.4	40.8	96.5	64.1	59.9	36.7	59.9	67.2	31.8	83.8	69.8	22.5	4
MNP 3.5 s/wk.	120.7	90.7	38.8	141.4	106.5	108.2	82.7	109.7	84.3	81.8	83.6	68.2	46.9	10
MNP 7 s/wk.	120.7	90.7	38.8	191.4	156.5	158.2	132.7	159.7	134.3	131.8	83.6	94.1	71.6	12
sq-LNS 3.5 s/wk.	118.8	105.9	65.9	141.4	77.5	92.7	62.6	78.7	58.3	59.4	133.6	60	67.3	7
sq-LNS 7 s/wk.	118.8	121.2	93.2	191.4	99	129.4	93.3	99.7	82.3	87	183.6	78.2	113	13
FBDR+ CF 1 s/wk.	244.4	126.1	93.7	152.7	103.5	173.9	75.1	114.7	102.4	120.8	221.1	131.2	44.6	12
FBDR+MNP3.5 s/wk.	239.3	125.4	92.6	202	149.6	224.2	126.1	162.6	146.7	170.8	221.1	146.4	67.3	12
FBDR+MNP 7 s/wk.	239.3	125.4	92.6	252	199.6	274.2	176.1	212.6	196.7	220.8	221.1	172.3	92	13
FBDR+ MNP 4 s/wk.[11]	239.3	125.4	92.6	209.1	156.8	231.3	133.3	169.8	153.8	177.9	221.2	150.1	70.8	13
FBDR+ sq-LNS 1 s/wk.	242.8	130.2	100.6	166.3	108.2	185.6	85.7	121.2	104.3	128.7	235.4	127.9	56.4	12
FBDR+CF1 s/wk. +MNP 3.5 s/wk.	242.1	126.8	92.9	202.7	151.3	223.3	124.2	162.9	151.2	170.8	221.1	151.5	68.1	12
FBDR+CF1 s/wk. +MNP7 s/wk.	242.1	125.8	92.9	252.7	201.3	273.3	174.2	212.9	201.2	220.8	221.1	177.4	92.8	13
FBDR+ CF+ sq-LNS	NP[12]	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0

[1] The optimal diet formulated by using goal programming (Optifood module II).
[2] Each diet sequentially maximizes each micronutrient (Optifood module III)
[3] Each diet sequentially minimizes each micronutrient (Optifood module III)
[4] Recommended nutrient intake for iron assuming 5% absorption
[5] Recommended nutrient intake for zinc assuming low absorption
[6] Number of nutrients that cover at least 70% of the recommended nutrient intake in the worst-case scenario.
[7] Nutritionally best possible diet (Optifood module II)
[8] Diet sequentially maximizes each nutrient (Optifood module III).
[9] Set of food based dietary recommendations selected
[10] Number of servings per week
[11] Best alternative option
[12] NP= Combination not possible due to energy constraints

Supplemental Table 12. The optimal[1], best-case scenario[2] and worst-case scenario[3] of the baseline diet; the worst-case scenario for the food based diet recommendations and alternative combinations expressed as a percentage of the recommended nutrient intake in 6 to 8 mo. children of SNNP region

	Protein	Fat	Calcium	Vit. C	Vit B-1	Vit B-2	Niacin	Vit. B-6	Folate	Vit. B-12	Vit. A	Iron[4]	Zinc[5]	N[6]
Baseline[7]	161.5	155.5	100	110.4	76.8	152.6	44.2	66.4	84.3	121.8	101.2	42.5	30	9
best-case scenario[8]	220.4	201.2	130.6	121.1	85.1	228.6	53.2	76.8	90.2	189.9	118.2	43.7	32.6	10
worst-case scenario	93.9	144.9	53.6	109.9	43.7	64.5	34	38.1	47.1	47.6	100.5	6.8	16.3	4
FBDR[9]	150.8	154.6	95.1	110.1	71.9	146.1	41.5	59.4	76	118.3	101.1	35.2	28.3	9
CF3.5 s/wk.[10]	100.9	145.3	54.3	112	47.9	66.2	37.4	40	67.4	47.6	100.6	6.5	16.9	4
CF 7 s/wk.	124.6	147.4	55.5	114.1	63.9	71.8	45.2	55	93.1	47.6	100.7	11	20.4	7
MNP 3.5 s/wk.	93.9	144.9	53.6	159.9	127.1	127	109	121.4	140.9	111.9	100.5	22.9	40.7	10
MNP 7 s/wk.	93.9	144.9	53.6	209.9	210.4	189.5	184	204.8	234.6	176.2	100.5	39	65.1	10
sq-LNS 3.5 s/wk.	93.7	166.5	88	159.8	83.1	110.7	80.2	76.9	92.1	83.1	150.5	18.6	61.2	11
sq-LNS 7 s/wk.	103.9	188.8	122.7	209.8	130.8	159.4	129.2	124.2	141.2	118.6	200.5	33.3	108.6	12
FBDR+ CF 1 s/wk.	157.9	155.4	95.5	110.7	76.6	147.8	43.7	63.8	83.5	118.3	101.2	26.6	29.3	9
FBDR+ MNP 3.5 s/wk.	150.8	154.6	95.1	160.1	155.2	208.6	116.5	142.7	169.8	182.5	101.1	51.2	52.7	11
FBDR+ MNP 7 s/wk.	150.8	154.6	95.1	210.1	238.5	271.1	191.5	226	263.5	246.8	101.1	67.4	77.1	12
FBDR+ sq-LNS 1 s/wk.	154.9	161.3	105.1	124.4	86.1	160.3	55.7	73.6	90.3	128.4	115.4	39.8	41.9	10
FBDR+CF 1 s/wk. +MNP 3.5 s/wk.	150.8	154.6	95.1	160.1	155.2	208.6	116.5	142.7	169.8	182.5	101.1	51.3	52.7	11
FDBR+CF1 s/wk. +MNP 7 s/wk.[11]	150.8	154.6	95.1	210.1	238.5	271.1	191.5	226	263.5	246.8	101.1	67.4	77.1	12
FBDR+ CF s/wk. + sq-LNS s/wk.	NP[12]	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0

[1] The optimal diet formulated by using goal programming (Optifood module II).
[2] Each diet sequentially maximizes each micronutrient (Optifood module III)
[3] Each diet sequentially minimizes each micronutrient (Optifood module III)
[4] Recommended nutrient intake for iron assuming 5% absorption
[5] Recommended nutrient intake for zinc assuming low absorption
[6] Number of nutrient that cover at least 70% of the recommended nutrient intake in the worst-case scenario.
[7] Nutritionally best possible diet (Optifood module II)
[8] Diet sequentially maximizes each nutrient (Optifood module III).
[9] Set of food based dietary recommendations selected.
[10] s/wk=number of servings per week
[11] Best alternative option
[12] NP= Combination not possible due to energy constraints

Chapter 3

Supplemental Table 13. The optimal[1], best-case scenario[2] and worst-case scenario[3] of the baseline diet; the worst-case scenario for the food based recommendations and alternative combinations expressed as a percentage of the recommended nutrient in 9 to 11 mo. children of SNNP.

	Protein	Fat	Calcium	Vit. C	Vit B-1	Vit B-2	Niacin	Vit. B-6	Folate	Vit. B-12	Vit. A	Iron[4]	Zinc[5]	N[6]
Baseline[7]	162.1	138.2	100.6	136	101.5	137.6	66.2	132.9	115.6	100	170.9	76.6	36.1	11
best-case scenario[8]	211.8	192.8	130.6	163.5	121.7	219.5	86.5	191.4	161.4	174.7	185.8	81.3	40.4	12
worst-case scenario	84.1	121.3	50.9	102.5	48	63.9	32.6	52.9	49.6	44.8	93.8	10.6	15.5	4
FBDR[9]	121.2	127.6	97.4	124.5	70.4	128	49	116.3	93	81.1	149.9	49.8	24.3	10
CF3.5 s/wk.[10]	92.3	122.4	51.4	104.7	51.9	66.4	37	53.7	69.3	44.8	93.9	9.9	16.8	4
CF 7 s/wk.	108.2	124.4	52.1	106.8	63.3	69.2	43.3	55.3	91	44.8	94	11.3	19.5	5
MNP 3.5 s/wk.	84.1	121.3	50.9	152.5	131.3	126.4	107.6	136.2	143.3	109.1	93.8	26.7	39.9	10
MNP 7 s/wk.	84.1	121.3	50.9	202.5	214.6	188.9	182.6	219.6	237.1	173.4	93.8	42.9	64.3	10
sq-LNS 3.5 s/wk.	85.2	141.4	85.2	152.5	87.8	110.9	79.6	91.2	94.6	80.3	143.8	22.3	61.3	12
sq-LNS 7 s/wk.	90.6	161.9	119.5	202.5	131.8	158.1	127.4	130	140	115.8	193.8	34.2	107.9	12
FBDR+ CF 3.5 s/wk.	143.6	129.9	98.7	128.6	87.5	134.3	57.6	131.1	118.6	81.1	150	54.8	27.9	10
FBDR+ MNP 3.5 s/wk.	121.2	127.6	97.4	174.5	153.8	190.5	124	199.6	186.8	145.4	149.9	65.9	48.7	11
FBDR+ MNP 7 s/wk.[11]	121.2	127.6	97.4	224.5	237.1	253	199	283	280.5	209.6	149.9	82.1	73.1	13
FBDR+ sq-LNS 1 s/wk.	124.8	133.5	107.4	138.8	84.6	142.2	63.3	130.3	107	91.2	164.2	54.4	37.9	9
FBDR+ sq-LNS 3.5 s/wk.	134	148.5	132.4	174.5	120.2	177.7	99	165.7	142.7	116.6	199.9	65.9	71.9	12
FBDR+CF3.5 s/wk. +MNP 3.5 s/wk.	143.6	129.9	98.7	178.6	170.8	196.8	132.6	214.4	212.4	145.4	150	71	52.3	12
FDBR+CF3.5 s/wk. +MNP 7 s/wk.	143.6	129.9	98.7	228.6	254.2	259.3	207.6	297.8	306.1	209.7	150	87.1	76.6	13
FBDR+ CF2 s/wk. + sq-LNS2 s/wk.	141.6	140.9	118.1	157.1	109.3	160.5	83.1	153.1	136.1	101.4	178.5	61.9	53.7	11

[1] The optimal diet formulated by using goal programming (Optifood module II).
[2] Each diet maximizes each micronutrient (Optifood module III)
[3] Each diet minimizes each micronutrient (Optifood module III)
[4] Recommended nutrient intake for iron assuming 5% absorption
[5] Recommended nutrient intake for zinc assuming low absorption
[6] Number of nutrient to reach at least 70% of the recommended nutrient intake in the worst case scenario.
[7] Nutritionally best possible diet (Optifood module II)
[8] Diet sequentially maximizes each nutrient (Optifood module III).
[9] Set of food based dietary recommendations selected.
[10] s/wk=number of servings per week
[11] Best alternative option

Supplemental Table 14. The optimal[1], best-case scenario[2] and worst-case scenario[3] of the baseline diet; the worst-case scenario for the food based recommendations and alternative combinations expressed as a percentage of the recommended nutrient intake in 12 to 23 mo. children of SNNP region.

	Protein	Fat	Calcium	Vit. C	Vit B-1	Vit B-2	Niacin	Vit. B-6	Folate	Vit. B-12	Vit. A	Iron[4]	Zinc[5]	N[6]
Baseline[7]	250.7	109.4	100	122.5	109.6	170.8	96	117.5	100	100	141.6	128.1	62.1	1
best-case scenario[8]	283.4	173	114.1	180.1	125.4	206.8	121.8	216.5	130.3	135.2	182.3	201.6	65.1	1
worst-case scenario	89.9	88.1	38.4	91.4	42.8	54.4	26.9	61	33.9	31.8	83.6	33	17	4
FBDR[9]	243.6	113.6	77.7	93.4	100	159.6	81.4	101.1	96.6	120.9	111.6	108.4	57.9	12
CF3.5 s/wk.[10]	102.6	88.9	38.7	94.6	45.6	56.7	29.5	52.5	49.6	31.8	83.7	33	19.4	4
CF 7 s/wk.	121.5	90.4	39.2	97.8	50.7	60	33.5	53.3	65.4	31.8	83.9	34.1	22.4	4
MNP 3.5 s/wk.	89.9	88.1	38.4	141.4	92.8	104.4	76.9	111	83.9	81.8	83.6	58.8	41.7	10
MNP 7 s/wk.	89.9	88.1	38.4	191.4	142.8	154.4	126.9	161	133.9	131.8	83.6	84.7	66.4	11
sq-LNS 3.5 s/wk.	90.9	103.6	65.5	141.4	66.4	91.3	57.2	70	57.9	59.4	133.6	51.9	63.6	6
sq-LNS 7 s/wk.	94.8	119.2	93	191.4	90.1	129	87.9	99	81.9	87	183.6	71.8	110.3	13
FBDR+ CF 1 s/wk.	252.5	114.4	78.2	94.4	104.2	161.7	83.7	105.1	102.5	120.9	111.6	111.9	59.5	12
FBDR+ MNP 3.5 s/wk.[11]	243.6	113.6	77.8	143.4	150	209.6	131.4	151.1	146.6	170.9	111.6	134.3	82.6	13
FBDR+ MNP 7 s/wk.	243.6	113.6	77.8	193.4	200	259.6	181.4	201.1	196.6	220.9	111.6	160.1	107.3	13
FBDR+ sq-LNS 1 s/wk.	254.6	120.8	92.9	110.3	111.1	178.1	93.3	112.7	106.2	134.5	127.1	125.5	73.7	13
FBDR+CF 1 s/wk. +MNP 3.5 s/wk.	252.2	114.4	78.2	144.4	154.2	211.7	133.7	155.1	152.5	170.9	111.6	137.8	84.2	13
FDBR+CF1 s/wk. +MNP 7 s/wk.	252.2	114.4	78.2	194.4	204.2	261.7	183.7	205.1	202.5	220.9	111.6	163.6	108.8	13
FBDR+ CF1 s/wk. + sq-LNS1 s/wk.	259.6	122	94.4	121	113.2	179.3	97	115.4	110.4	135.7	137.7	131.2	70.4	13

1 The optimal diet formulated by using goal programming (Optifood module II).
2 Each diet maximizes each micronutrient (Optifood module III)
3 Each diet minimizes each micronutrient (Optifood module III)
4 Recommended nutrient intake for iron assuming 5% absorption
5 Recommended nutrient intake for zinc assuming low absorption
6 Number of nutrients to cover at least 70% of the recommended nutrient intake in the worst-case scenario
7 Nutritionally best possible diet (Optifood module II)
8 Diet sequentially maximizes each nutrient (Optifood module III).
9 Set of food based dietary recommendations selected.
10 s/wk=number of servings per week
11 Best alternative option

Chapter 4

Effectiveness of a programme intervention with reduced-iron multiple micronutrient powders on iron status, morbidity and growth in young children in Ethiopia

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Abstract

Background: Despite the potential for improving iron status and child growth in low- and middle-income settings, concerns on the safety of high iron dosages of Micronutrient Powders (MNPs) currently limit their applicability in programs. The objective of this study was to assess the effectiveness of an integrated program with low iron dose (6 mg/serving) MNPs among children 6-23 months of age in Ethiopia.

Methods: We examined the effectiveness and risks of an integrated complementary feeding program with low iron dose (6 mg/serving) MNPs among 6-23 months old Ethiopian children using a quasi-experimental study design comparing children from 5 intervention districts (n=1172) to those from 4 matched non-intervention districts (n=1137) (ClinicalTrials.gov, NCT02479815).

Results: Haemoglobin concentrations increased in intervention and decreased in non-intervention children (group-difference +3.17g/L), but without improvement in iron stores. Intervention children were 2.31 times more likely to have diarrhoea and 2.08 times more likely to have common cold and flu, but these differences decreased towards the end of the intervention. At end line, intervention children had higher mean Height-for-Age Z score (HAZ) and a 51% reduced odds of being stunted compared to non-intervention children.

Conclusions: MNPs with low iron dose, when provided combined with other Infant and Young Child Feeding (IYCF) interventions, marginally improved haemoglobin status and resulted in a remarkable improvement in linear growth in 6-23 month old children. These benefits likely outweigh the relative small increase in risk of diarrhoea, which seemed mostly mild in nature and disappeared over time.

Introduction

Micronutrient deficiencies are a global health burden, especially for young children in developing countries, because of poor quality diets and frequent infectious diseases. The high prevalence of deficiencies and their important adverse consequences on mortality, morbidity and disability result in a substantial disease burden. In particular, deficiencies of vitamin A and zinc increase the risk of child mortality, and zinc deficiency increases infectious morbidity and reduces linear growth as well. Deficiencies of iodine and iron are significant primarily for their effects on development and cognition and consequent disabilities[1, 2]. Overall, it has been estimated that micronutrient deficiencies account for about 7.3% of the global burden of disease, with iron and vitamin A deficiency ranking among the 15 leading causes of the global disease burden[3]. The World Health Organisation (WHO) recommends daily supplementation with multiple micronutrient powders (MNP) for all young children in populations with a prevalence of childhood anaemia greater than 20% and when the diet does not include fortified foods[4]. Home fortification of foods with powders containing multiple micronutrients is recommended as an alternative to increase the vitamin and mineral intake in children 6–23 months of age, because micronutrient deficiencies often co-exist, and plant-based diets, commonly being consumed by low-income households, generally provide insufficient amounts of key micronutrients to meet the recommended nutrient intakes for young children[1].

Home fortification with iron-containing MNPs has been shown to reduce both anaemia and iron deficiency anaemia (IDA) in infants and young children[5]. Because of its potential to reduce anaemia and improve micronutrient intakes, MNPs are increasingly being used in Infant and Young Child Feeding (IYCF) programs in low- and middle-income countries. However, concerns around the safety of iron-supplement interventions among iron-replete children in both malaria-endemic and malaria-free areas have arisen, as the daily provision of supplemental doses of iron may exacerbate the presence and severity of infections, including malaria and diarrhoea[6-8]. The observed increased risk of infectious diseases may have been caused in part by an increase in pathogenic bacteria in the gut due to unabsorbed iron[8]. These studies have invigorated the debate around the safety of (daily) iron interventions particularly in very young children, with adequate iron status, who may not yet have the capacity to adequately regulate iron absorption. Also in Ethiopia, with 34% of 6-59 months children having anaemia and 9% having IDA in 2016, the high iron intakes found in the Ethiopian national food consumption survey of 2013 have raised questions regarding necessity and safety of additional iron interventions. A low-dose iron supplementation may therefore be preferred to reduce side effects[9], but it is unclear to what level the daily iron dose in MNP can be reduced to retain efficacy against anaemia and at the same time reduce the adverse impact on morbidity.

Previous studies conducted in Ghana, Cambodia and Bangladesh, with similar settings and infection rates as in Ethiopia, used multiple micronutrient supplements including 12.5 mg of elemental iron per serving, among children aged 6-18 months[7-13]. In both settings, daily use of MNP with iron did not result in an increased incidence of malaria or other infectious diseases and was effective for preventing or treating anaemia. Lower dosages (6 mg iron per daily serving) were found to be efficacious in improving iron status in a trial involving small-quantity Lipid-Based Supplements (Sq-LNS, 20 g lipid-based spreads to be used as a home fortificant) in Burkina Faso without increase in incidence of diarrhoea and malaria[14]. None of these studies, however, evaluated the use of a lower dose iron MNP in a scaled-up program context with limited control over intake and compliance.

We assessed the effectiveness as well as risks and benefits of a low-dose iron MNP (6 mg iron per serving every other day) on iron status, morbidity and growth of Ethiopian infants and young children within the context of a program on local CF production.

Methods

Study design and participants

Within the Ethiopian community based nutrition program, the organisation Nutrition International (NI), together with UNICEF and implementing partners, implemented a local complementary food (CF) production (Grain Bank) program to improve the quality of CF and IYCF practices in four regions (Amhara, Oromia, Tigray and South Nations and Nationalities and Peoples (SNNP)) in Ethiopia[15]. Our MNP study was conducted in two of the four program regions, Oromia and SNNP. We employed a quasi-experimental matched-control design in which outcomes were compared between children of intervention and non-intervention *kebeles* (clusters). In SNNP 3 out of 5 and in Oromia 2 out of 5 Grain Bank program *woredas* (districts) were included as intervention districts because of large population size. Per intervention district 3-6 villages were selected based on status of grain bank in the village, number of children below 12 months of age and accessibility during rainy season. These so-called intervention villages (n=17) were matched with 18 non-intervention villages in a 1:1 ratio (for 1 district on a 1:2 ratio due to large size of intervention district) based on pre-set criteria including similar geographical and ecological conditions, existence of other health- or nutrition programs, and livelihood data.

Primary outcomes were Haemoglobin (Hb), anaemia and diarrhoea. Secondary outcomes were other iron status indicators (serum ferritin (SF), iron deficiency (ID), iron deficiency anaemia (IDA)), morbidity of other diseases (common cold and flu, and measured fever) and growth including Height-for-Age Z-score (HAZ), Weight-for-Height Z-score (WHZ), Weight-for-Age Z-score (WAZ), and Height-for-Age Difference (HAD).

The sample size was calculated based on Hayes and Bennett[16]. We assumed a 11.7% incidence of diarrhoea in children 0-2 years of age among children in the non-intervention area[17]. We expected a 12% increase in the incidence of overall diarrhoea in the intervention group (assumed incidence of 5.3 episodes per year per child). This assumed effect was based on the observed Incidence Rate Ratio (IRR) of 1.12 for overall diarrhoea after introduction of MNP in a large effectiveness study in Pakistan[6], as this was the largest study to date to observe an adverse effect on diarrhoea after MNP supplementation. A sample size of 1170 per group would enable us to detect this increase of incidence of overall diarrhoea with 80% power and two-sided p-value of 5% with an assumed drop-out rate of ten percent.

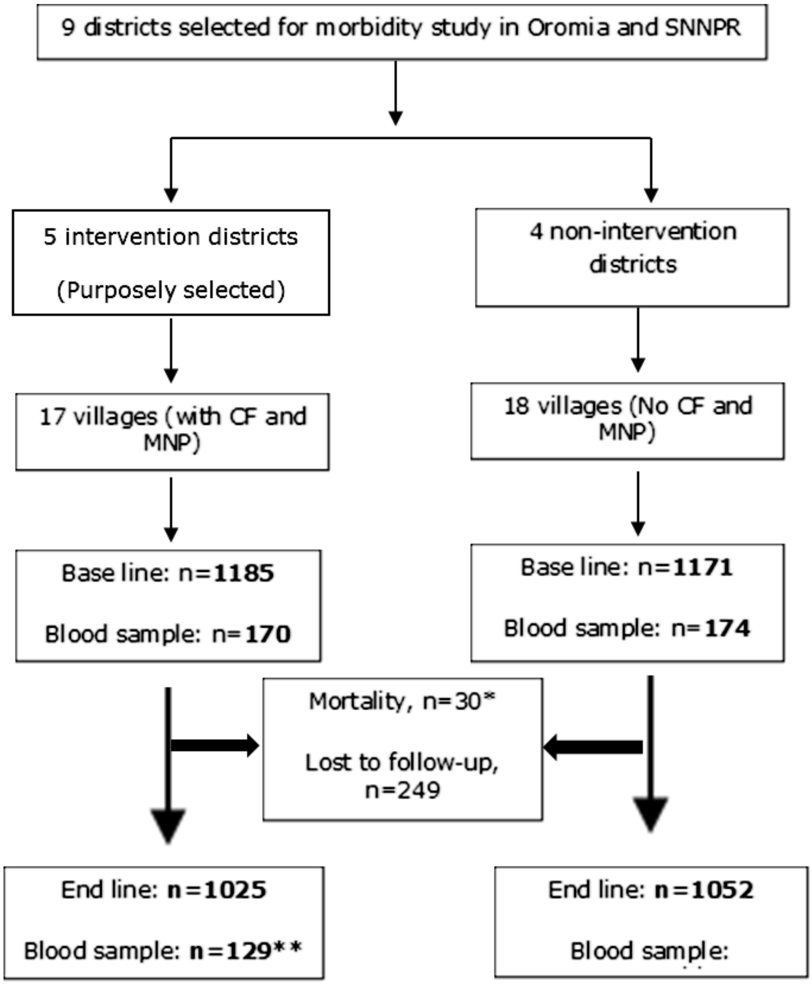

Figure 1. Study profile

* Thirty children died (5 from Intervention villages before the MNP intervention started and 25 from non-intervention villages throughout the study period)

** End line blood samples were taken from 259 of the 344 children with blood samples collected at baseline: 41 were absent, 1 was a severe-acute-malnutrition case, 2 were transferred and 41 refused to give a blood sample. SNNPR: Southern Nations, Nationalities and Peoples' Region; CF: complementary food; MNP: multiple micronutrient powder; *n*= number of children.

For anaemia we assumed a prevalence of 73% in 6-11 month old Ethiopian children based on 2012 data from the Ethiopia Demographic and Health Survey, and expected to observe a 30% decrease in anaemia concentration, which was the average reduction in anaemia prevalence observed in a systematic review of studies with iron-containing multiple micronutrient powders[5]. Based on a power of 80%, a two-sided p-value of 5%, a ten percent drop-out rate and design effect of two for the matched-controlled design, we aimed to collect biochemical data on 130 children in the control and 130 in the intervention group.

Target children were aged 6-11 months at baseline to ensure that all children would benefit from the program intervention for the entire duration of the follow-up. After listing all children below one year of age in each selected village by health extension workers, parents were informed and invited to bring their child for screening. Per village, about 65 eligible children were included in the study, a total of 2356 children, 1185 in the intervention group, which received low-dose iron MNPs (30 sachets/two months) along with the CF from the Grainbank program, and 1171 in the non-intervention group, which did not receive MNPs and CF (Figure 1). The sub-sample for biochemical assessment was selected from these study children by going from study village to village, starting nearby the capital Addis Ababa, until the required number was obtained.

Data collection procedures

The study was conducted from March 2015 to May 2016 during which children were each followed for 52 weeks. Due to a delay in the delivery of MNPs children did not receive these during the first 15 weeks after end of baseline investigation, with a mean duration of this pre-intervention period of 93 ± 14.8 days. After this period the MNP intervention was implemented for 37 weeks with a mean duration of intervention period of 182 ± 32.6 days. The MNP intervention product MixMe® was manufactured by DSM Nutritional Products in South Africa. Each sachet of MixMe® contained 6 mg of iron as encapsulated ferrous fumarate, instead of the usual 12.5 mg iron, and 14 other essential vitamins and minerals, see Table 1.

The study team provided MNPs at the local health post. Mothers/caregivers were given 30 sachets every 2 months and were instructed to administer 15 sachets per month to their children, one sachet every other day. Children were thus supposed to consume 6 mg of iron every other day. During monthly home visits, compliance and adherence were assessed by counting empty sachets. Overall, children consumed an average of 79% of the total servings of MNPs received, during the intervention period.

Table 1. Minerals and vitamins contents of MixMe per serving (1 g sachet).

Nutrient	Per 1g
Vitamin A	1332 IU / 400 mcg
Vitamin D	200 IU / 5 mcg
Vitamin E	5 mg TE
Vitamin B_1	0.5 mg
Vitamin B_2	0.5 mg
Vitamin B_6	0.5 mg
Vitamin B_{12}	0.9 mcg
Niacin amide	6 mg
Folate	150 mcg
Vitamin C	30 mg
Iron	6 mg
Zinc	4.1 mg
Copper	0.56 mg
Selenium	17 mcg
Iodine	90 mcg

IU: International Unit; mcg: microgram; mg: milligram; TE: Tocopherol Equivalent.

Thirty-six well-trained data collectors and six field supervisors carried out data collection. Children who required medical treatment were referred to the nearest health facility. A data safety and monitoring board (DSMB) was constituted, consisting of a paediatrician, a physician and a public health scientist, all independent to the study. All adverse events were communicated to the DSMB within a maximum of two days.

Morbidity from infectious diseases such as diarrhoea, flu, and fever was assessed every two weeks by means of a pretested recall questionnaire. Children’s body temperature was measured every two weeks in the armpit using a digital thermometer with the precision of ± 0.1 °C (SLC, TempCheck) and a child with a body temperature above 37.5°C was referred to the health center for malaria testing, further investigation and treatment.

Measurements of height, and weight were taken every quarter using standard procedures[18]. Height was measured on the UNICEF standard measuring board with a precision of 0.1 cm; weight was measured using UNICEF Seca 874 U electronic scales (UNICEF Supply Division, Copenhagen, Denmark) with 100 g precision, calibrated daily with a known weight. Children shorter than 85 cm were measured lying down, while those greater than or equal to 85 cm were measured standing up. Two measurements were taken. A third one was repeated if the difference between the first two was more than 0.5 cm or 0.5 kg.

Iron status, haemoglobin (Hb), serum ferritin (SF), soluble transferrin receptor (sTfR), and inflammation markers, high sensitive C-reactive protein (CRP) and α1-acid glycoprotein (AGP), were measured at baseline- and end line in a subsample of children. For this purpose venous blood samples (3 ml trace element-free vacuettes and EDTA tubes) were collected at the health post of the study villages by highly skilled phlebotomists following the WHO blood collection protocol[19]. Samples were transported in cold boxes containing frozen gel packs (< -18°C) to a nearby health center or hospital for serum separation and aliquoting in cryovials. Serum samples were stored in deep freezers of the regional laboratories until transported to the Ethiopian Public Health Institute (EPHI) for storage at -80°C and subsequent laboratory analyses after the final end line sample was obtained. Hb was analysed immediately (in the field) using a Hemocue® photometer (Hb 301, Hemocue, Angelholm, Sweden). Hb concentration was corrected for altitude using Global Positioning System (GPS) data for the villages and altitude adjustment values as provided by the International Nutritional Anemia Consultative Group (INACG)[20]. Serum ferritin was analysed using Cobas e411 (Roche Diagnostics GmbH), a fully automatic run-oriented immunoassay analyser for the determination of immunological tests using the electrochemiluminescence immunoassay ECLIA process[21]. The concentrations of CRP, sTfR and AGP were analysed using Cobas 6000 (Roche Diagnostics, GmbH, Mannheim, Germany), using the immunoturbidimetric principle. The coefficients of variation (CV) (inter-assay) for the various indicators were 6.7% for SF, 4.7% for CRP, 2.1% for sTfR, and 4.2% for AGP.

All the questionnaires were manually checked for completeness before data entry in duplicate using CsPro 5.0 software(United States Census Bureau, Suitland, MD, United States).

Statistical analysis

Statistical analysis was done with SPSS version 22.0(IBM Corporation, Armonk, NY, United States). The analyses followed the intention to treat principle. Data distributions were checked by visual examination of Q-Q plots, histograms and tested for normality with the Kolmogorov-Smirnov test. Baseline characteristics of study children and their caregivers were summarized as mean (SD) for continuous variables which were normally distributed, or otherwise as median (25^{th} and 75^{th} percentiles), and as percentages for categorical variables. Descriptive data on intervention and non-intervention children were compared using the independent sample t-test for continuous variables, Mann-Whitney *U* test for skewed continuous variables and chi-square test for categorical variables.

For morbidity calculations, each randomized child contributed to the total number of observation days until they were lost to follow-up or until completion of the intervention. Fever was defined as body temperature >37.5°C. The longitudinal prevalence of each illness, diarrhoea, common cold/flu, and fever, was calculated, dividing the total number of days being ill by the total days of observation per child, multiplied by 100. Additionally, we calculated the incidence rate per year for diarrhoea and common cold/flu as the number of sick cases per total number of children at the given time based on the study period and extrapolated to one year. This was based on the assumption that children would have experienced maximum one episode per recall period of 14 days. Morbidity was calculated during the pre-intervention period and intervention period separately. Differences in longitudinal prevalence of diarrhoea, common cold/flu, and measured fever were analysed with Generalized Linear Mixed Models (GLMM) adjusted for baseline values, age, gender, and treatment group. The morbidity observed during the pre-intervention run-in period was used as a proxy for baseline morbidity. To adjust for the matched-controlled design of the study, a proxy for matched pairs of districts were included in the models as random effects. Differences in diarrhoea and common cold/flu prevalence over time were analysed with GLMM using prevalence per 2 weeks observation round as dependent variable, and adjusting for interaction with time, baseline values, age, gender, and treatment group. Differences in incidence from diarrhoea and flu, and number of clinical visits, were analysed with Poisson regression using the number of episodes or clinic visits as the dependent variable, baseline incidence (diarrhoea and common cold/flu), age at baseline, gender, matching pairs and treatment groups as covariates, and including the total number of observation days as an offset term.

Anaemia was defined as Hb <110g/L and ID was defined as SF concentration <12μg/L. IDA was defined as Hb <110g/L with SF<12μg/L[21]. Inflammation was defined as CRP>5mg/L and/or AGP>1.0g/L[22]. The Biomarkers Reflecting Inflammation and Nutritional Determinants of Anaemia (BRINDA) internal regression correction (IRC) approach was used to correct SF concentrations for inflammation,[22] using a separate regression coefficient for intervention and non-intervention groups. The effect of the intervention on iron status was tested for the subsample of children with base- and endline data, using linear regression analyses using change in altitude adjusted Hb, SF adjusted for inflammation, or sTfR as the dependent variable, and age, gender as covariates.

Weight-for-age (WAZ), length/height-for-age (HAZ), and weight-for-height (WHZ) were determined using WHO Anthro-Plus software version 3.2.2 based on 2006 WHO reference population[18]. Height-for-age differences (HAD) in cm was calculated by subtracting the median height (sex-and age specific based on the WHO 2006 growth standards) from the measured height of the child[23]. During baseline data cleaning 25 children with WHZ z-scores < -3.01 were excluded as not meeting inclusion criteria and 1 child was excluded from further analysis because of implausible value for z-score (>9.0). Linear Mixed Models (LMM) were used to compare longitudinal results of anthropometry between intervention and non-intervention children. Subject-level random effects were introduced to account for individual growth trajectories. After comparing the Akaike information criterion (AIC) values for model selection, we used the autoregressive model (AR1) for repeated effects and Variance Components (VC) for random effects. Time-trend interactions were analysed in the Linear Mixed Models to assess whether differences between treatment groups changed over time.

Differences between groups in categorical variables at end line were compared using logistic regression adjusting for age, gender and baseline values for anaemia, ID, and IDA, and adjusting for age, gender, matching-pair and baseline values when studying stunting, wasting, and underweight. Tests of significance were 2-tailed, and $p<0.05$ was considered statistically significant.

Ethics approval and consent to participate

Ethical approval was obtained from the Ethiopian National Research Ethics Review Committee (NRERC). Signed consent was obtained from caregivers of the study children before participation in the study. The study was registered at http://www.clinicaltrials.gov/ with clinical trials identifier of NCT02479815.

Results

Baseline data were available for 2309 children of age 6-11 months from 17 intervention (n=1172) and 18 non-intervention (n=1137) villages. For biomarker analysis, a subgroup of 129 children from each group was analysed. Socio-economic characteristics of mothers and children were similar at baseline (Table 2). A majority of the study children were still breastfed (>93%). Mean age of mothers was 25.3 ± 5.8 year in the intervention group and 25.7 ± 5.7 year in the non-intervention group. Half of the mothers were illiterate (about 45-50%); more than 90% of the households owned land.

Table 2. Baseline characteristics of the study participants[1].

Characteristics	**Intervention** *n*=1172		**Non-intervention** *n*=1137	
Region, Oromia (%)	50.1		49.3	
Child characteristics				
Gender, Female (%)	49.4		47.5	
Age (mo)	7.9	(1.8)	8.1	(1.9) *
Hb (g/L)[2]	112.4	(12.6)	115.0	(9.7) **
SF (µg/L)[3]	13.90	(6.57,24.07)	13.95	(8.88,23.74) **
sTfR (mg/L)[4]	5.97	(5.01,7.86)	5.44	(4.65,6.78) **
AGP(g/L)[5]	0.94	(0.70,1.18)	1.22	(0.93,1.60)
CRP (mg/L)[5]	1.52	(0.58, 4.81)	2.45	(0.91,5.97)
Mother's characteristics[6]				
Mother age (y)	25.3	(5.8)	25.7	(5.7)
Education, Illiterate (%)	49.9		44.8	*
Household characteristics				
Toilet facility - Pit latrine (%)	95.7		90.1	**
Access to safe drinking water (%)[7]	93.2		92.3	
Land ownership[8] (%)	90.8		91.1	

[1]Values are mean (SD), percent, or median (25th and 75th percentiles);
[2]Altitude adjusted, *n*=129 intervention, *n*=129 non-intervention;
[3]Adjusted for inflammation using the Biomarkers Reflecting Inflammation and Nutritional Determinants of Anaemia (BRINDA) Internal Regression Correction (Namaste et al., 2017). n=109 intervention, n=120 non-intervention;
[4]*n*=101 intervention, *n*=118 non-intervention;
[5]*n*=109 intervention, *n*=120 non-intervention;
[6]*n*=1171 for intervention and 1136 for non-intervention group;
[7]Safe drinking water includes piped water (public tap and private tap), protected spring, protected well, water from borehole (in the yard and public), water from truck and rainwater[24].
[8] Although theoretically in Ethiopia, land ownership always lies with the government, most families do have their own farming land to plough and produce agricultural produce.
*$p<0.05$, ** $p<0.001$ difference between intervention and non-intervention tested with t-test for normally distributed variables, Mann-Whitney *U* test for not normally distributed variables, Chi-square for categorical variables.

Iron status

At baseline, Hb concentration was lower in intervention (112.4 ± 12.6 g/L) compared to non-intervention children (115.0 ± 9.7 g/L) (Table 3). At the end of the intervention period, Hb levels were 114.8 ± 10.5 g/L in the intervention group and 114.2 ± 8.7 g/L in the non-intervention group. Hb concentrations increased in children in the intervention group (+2.40±1.17 g/L), and slightly decreased in children in the non-intervention group (-0.77 ±1.17 g/L) with a borderline significant difference in difference estimate of 3.17g/L (SE 1.65g/L, p=0.056) between intervention and non-intervention group. In contrast, SF concentrations increased in the non-intervention group (+6.42 ± 1.48 ug/L) between base- and end line, whereas they decreased in the intervention group (-2.10 ± 1.55 ug/L) resulting in a significant difference in difference estimate of -8.53 ug/L (SE 2.14 ug/L, p<0.001). sTfR concentrations decreased in both intervention and non-intervention groups, with no difference between groups (Table 3).

Table 3. Change in iron status during the intervention period[1].

	Intervention		**Non-Intervention**		**β(SE)[2]**		***P*-Value**
Hb (g/L)[3]							
Baseline	112.4	(12.6)	115.0	(9.7)			
Endline	114.8	(10.5)	114.2	(8.7)			
Change[4]	2.4	(1.17)	-0.8	(1.17)	3.17	(1.65)	0.056
SF(ug/L)[5]							
Baseline	13.9	(6.6,24.1)	14.0	(8.9,23.7)			
Endline	11.1	(5.8,22,6)	19.1	(11.0,35.6)			
Change[4]	-2.1	(1.6)	6.4	(1.5)	-8.53	(2.14)	<0.0001
sTfR(mg/L)[6]							
Baseline	6.0	(5.0,7.9)	5.4	(4.7,6.8)			
Endline	5.0	(4.1,6.2)	4.2	(3.7,4.7)			
Change[4]	-1.5	(0.4)	-1.6	(0.3)	0.11	(0.49)	0.820

[1]Values are mean (SE) or median (25th,75th percentiles), Change is calculated as end line minus baseline;
Hb: Haemoglobin (altitude adjusted); SF: serum ferritin (adjusted for inflammation using the Biomarkers Reflecting Inflammation and Nutritional Determinants of Anaemia (BRINDA) Internal Regression Correction (Namaste et al., 2017)); sTfR: serum transferrin receptor;
[2]Regression coefficient (SE) comparing intervention with non-intervention group in Generalized Linear Model (GLM) analysis with change in Hb, SF, and sTfR as dependent variable, gender and treatment group as fixed factors and age at baseline as covariate;
[3]*n*=129 for intervention and *n*=129 for non-intervention;
[4]Change is calculated as end line minus baseline;[5]*n*=108 for intervention and *n*=118 for non-intervention;
[6]*n*=101 for intervention and *n*=118 for non-intervention.

The prevalence of anaemia and IDA reduced in intervention children, from 35.7 to 24.8% for anaemia and from 27.0 to 14.5% for IDA, while they both increased slightly in non-intervention children (Figure 2). Adjusting for baseline prevalence, the end line prevalence of anaemia (OR 0.76, 95% CI 0.44-1.33) and IDA (OR

1.09, 95% CI 0.49-2.43) were not significantly different between the treatment groups. In contrast, the prevalence of ID increased significantly in intervention children (from 42.4 to 52.3%) and decreased in non-intervention children (from 40.8 to 30.5%, OR for ID at end line: 11.3; 95% CI: 3.7-34.1).

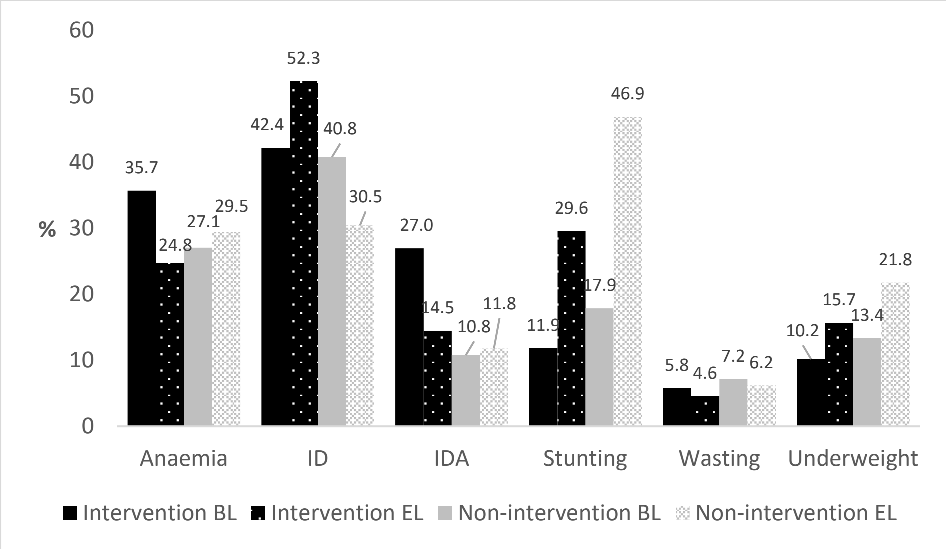

Figure 2. Prevalence of Anaemia, Iron Deficiency (ID), Iron Deficiency Anaemia (IDA), Stunting, Wasting and Underweight at baseline (BL) and end line (EL) in intervention and non-intervention groups[1].

[1]Differences in end line prevalence between intervention and non-intervention groups were tested with Logistic Regression, adjusted for age, gender, baseline prevalence (and matched pairs for stunting, wasting and underweight).

Morbidity

During the pre-intervention period, the mean (± SD) longitudinal prevalence of both diarrhoea (6.9±6.8% vs 4.9±6.8%, β=1.91, 95%CI: 1.38-2.45) and common cold and flu (8.0±8.4% vs 5.0±8.7%, β=2.98, 95%CI: 2.33-3.62) were significantly higher in the intervention compared to the non-intervention group. During the intervention period we observed a significantly higher longitudinal prevalence of diarrhoea in the intervention group (2.7±3.6%) compared to the non-intervention group (1.5±3.2%, β=1.01, 95%CI: 0.73-1.29) (Table 4). The average number of days of diarrhoea per episode was 4.7±2.2 and 4.2±1.8 ($p<0.001$), in the intervention and non-intervention children respectively. Similarly, for common cold/flu a significantly higher longitudinal prevalence (5.4±5.4%) was observed in the intervention children compared to the non-intervention children (2.7±3.7%, β=2.44, 95%CI 2.08-2.80). There was no difference in longitudinal prevalence of (measured) fever between groups (β=-0.01, 95%CI: -0.03-0.01).

Table 4. Prevalence and incidence of diarrhoea, common cold and flu, and fever during the intervention period.

Variable	**Intervention (*n* = 1148)**	**Non-Intervention (*n* = 1125)**	
Longitudinal Prevalence (%) [2]			**β (95% CI) [1]**
Diarrhoea	2.7 (3.6)	1.5 (3.2)	1.01(0.73,1.29) *
Common cold and flu	5.4 (5.4)	2.7 (3.7)	2.44(2.08,2.80) *
Fever	0.1 (0.2)	0.1 (0.3)	−0.01(−0.03,0.01)
Incidence Rate (per child/ year) [4]			**IRR (95% CI) [3]**
Number of observation days	204,456	210, 686	
Diarrhoea	2.67 (1,474)	1.34 (786)	2.31 (1.92;2.78) *
Common cold and flu	3.77 (2,178)	1.90 (1,109)	1.43 (1.23;1.65) *
Clinic visits due to diarrhoea (per year)[5]	0.41 (470)	0.37 (415)	1.23 (0.86,1.77)
Clinic visits due to common cold and flu (per year)[5]	0.30 (349)	0.38 (431)	0.90(0.62,1.32)

[1] Regression coefficient expressing difference in longitudinal prevalence (i.e. % of days sick out of total number of observation days) between intervention and non-intervention groups from Generalized Linear Mixed Models (GLMM) using age, gender, pre-intervention outcomes and matching pairs as covariates;

[2]Values are mean percentage (SD);

[3]IRR= Incidence Rate Ratio, 95%CI = 95% Confidence Interval, from Poisson regression using number of episodes as dependent variable, pre-intervention morbidity cases (diarrhoea and flu case), age, gender, and matching pairs as covariates. IRR of clinic visits were analysed with Poisson regression using number of clinic visits as dependent variable and age, gender and matching pairs as covariates;

[4]Mean incidence/child/year (total number of episodes) for incidence rate.

[5]Average number of clinic visits per child per year (total # of clinic visits for the group).

* P <0.001

During the intervention period, the incidence of diarrhoea was higher in the intervention compared to the non-intervention children (incidence rate ratio IRR: 2.31, CI95%: 1.92-2.78). A higher incidence was also observed for common cold/flu (IRR: 1.43, CI95%: 1.23-1.65). However, the incidence of clinic visits due to diarrhoea or common cold/flu were not different. The point prevalence at every 2 week visit for diarrhoea and common cold/flu in intervention and non-intervention children is shown in Figure 3. The differences between groups in point prevalence of diarrhoea and common cold and flu decreased over time ($p<0.001$ for interaction with time).

Growth

Over the course of the intervention, children in the intervention group had a significantly higher length and weight gain than children in the non-intervention group (Table 5). At end line mean HAZ was higher in intervention children compared to non-intervention children (adjusted β for difference in difference estimate: 0.18, SE: 0.05, $p<0.005$, Table 5), and similar results were observed for HAD ($\beta=0.78$, SE:0.12, $p<0.005$). No differences in end line WAZ ($\beta=0.01$, SE:0.04, $p=0.78$) and WHZ ($\beta=-0.09$, SE:0.05, $p=0.052$) were observed. The changes in HAZ and HAD between intervention and non-intervention group seemed to increase over time (Figure 4) and differences seemed to become larger after the second measurement which marked the start of MNPs distribution. In contrast, the differences in WHZ between intervention and non-intervention seemed to decrease over time, while there was no change in differences in WAZ between the groups over time (Figures 4c and 4d).

The prevalence of stunting, wasting and underweight increased over time in both groups (Figure 2). However, a significantly smaller increase in stunting was observed in the intervention compared to the non-intervention group (+17.7% vs. +29.0%, OR for stunting at end line =0.49; 95%CI: 0.40-0.60). A similar result was observed for underweight (+3.2% vs +6.1%; OR for underweight at end line: 0.61; 95%CI: 0.47-0.79), whereas the change in wasting was not different between groups (OR at end line: 0.75; 95%CI: 0.50-1.11).

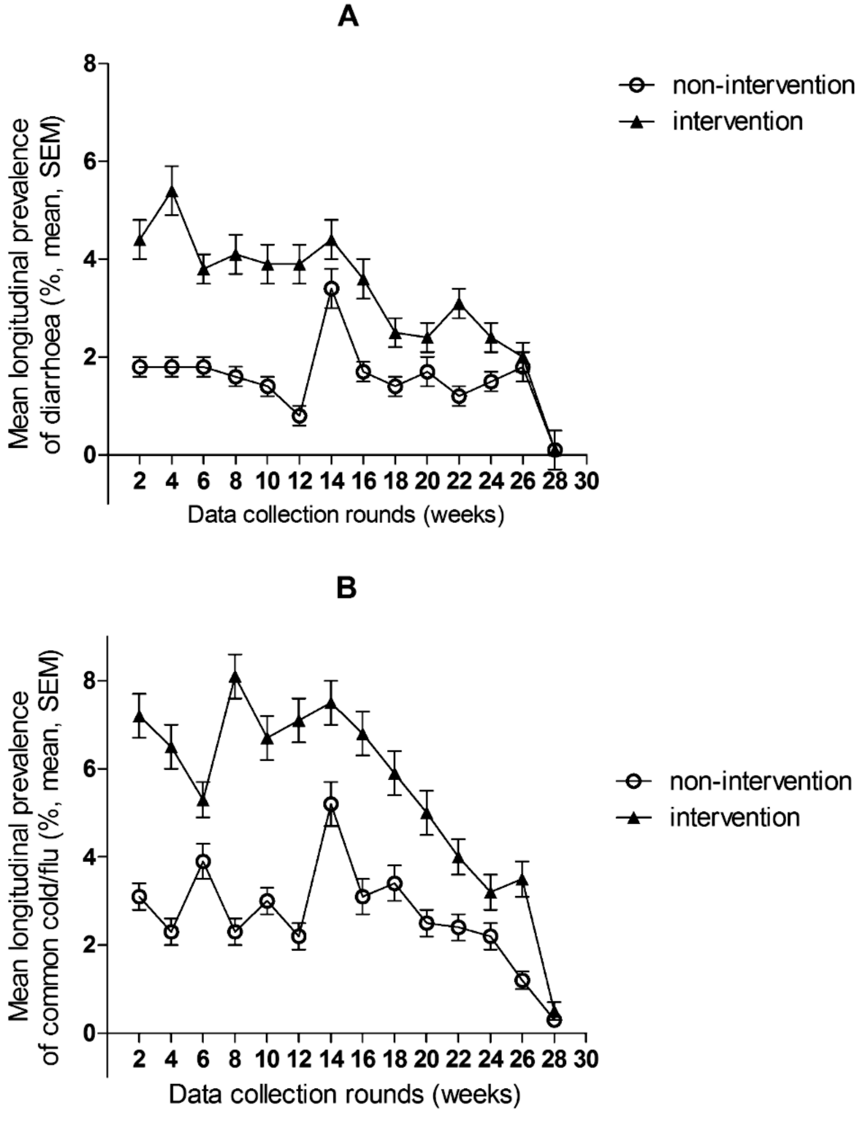

Figure 3. Mean longitudinal prevalence of diarrhoea (A) and common cold/flu (B) in intervention and non-intervention group over time at every 2 week measurement round. SEM = Standard Error of the Mean.

Table 5. Growth status of children during the intervention period[1].

	Intervention		Non-intervention		β(SE)[2]	
Height, cm						
Baseline	68.4	(3.8)	67.9	(4.0)		
1st Quarter	73.6	(3.6)	72.7	(3.9)	0.55	(0.09)**
2nd Quarter	77.2	(3.8)	76.1	(3.9)	0.67	(0.11)**
End line	80.0	(3.9)	78.8	(4.0)	0.77	(0.13)**
Weight, kg						
Baseline	7.8	(1.1)	7.6	(1.1)		
1st Quarter	8.9	(1.2)	8.6	(1.2)	0.15	(0.03)**
2nd Quarter	9.6	(1.2)	9.3	(1.2)	0.13	(0.04)**
End line	10.2	(1.3)	9.9	(1.3)	0.08	(0.04)*
HAZ						
Baseline	-0.49	(1.37)	-0.80	(1.43)		
1st Quarter	-1.12	(1.26)	-1.53	(1.35)	0.10	(0.04)*
2nd Quarter	-1.31	(1.24)	-1.80	(1.29)	0.18	(0.04)**
End line	-1.43	(1.22)	-1.91	(1.27)	0.18	(0.05)**
WHZ						
Baseline	-0.27	(1.08)	-0.42	(1.13)		
1st Quarter	-0.22	(1.06)	-0.43	(1.14)	0.04	(0.04)
2nd Quarter	-0.19	(1.00)	-0.33	(1.02)	-0.02	(0,04)
End line	-0.24	(1.03)	-0.31	(1.14)	-0.09	(0.05)
WAZ						
Baseline	-0.54	(1.27)	-0.83	(1.15)		
1st Quarter	-0.70	(1.11)	-1.08	(1.15)	0.07	(0.03)*
2nd Quarter	-0.76	(1.06)	-1.11	(1.06)	0.06	(0.04)
End line	-0.88	(1.05)	-1.18	(1.10)	0.01	(0.04)
HAD						
Baseline	-1.11	(3.13)	-1.81	(3.28)		
1st Quarter	-2.84	(3.22)	-3.89	(3.42)	0.33	(0.09)**
2nd Quarter	-3.61	(3.41)	-4.97	(3.55)	0.66	(0.11)**
End line	-4.20	(3.61)	-5.65	(3.71)	0.78	(0.12)**

[1]Values are mean (SD) unless stated otherwise; HAZ: Height for Age Z-score; WHZ: Weight for Height Z-score; WAZ: Weight for Age Z-score; HAD: Height for Age difference based on 2006 World Health Organization (WHO) reference population[25].

2Regression coefficient (SE) for interaction between time and treatment group with baseline as reference from LMM of growth status adjusting for age at baseline, gender, and matching pairs; *p value <0.05; **p value<0.001.

Chapter 4

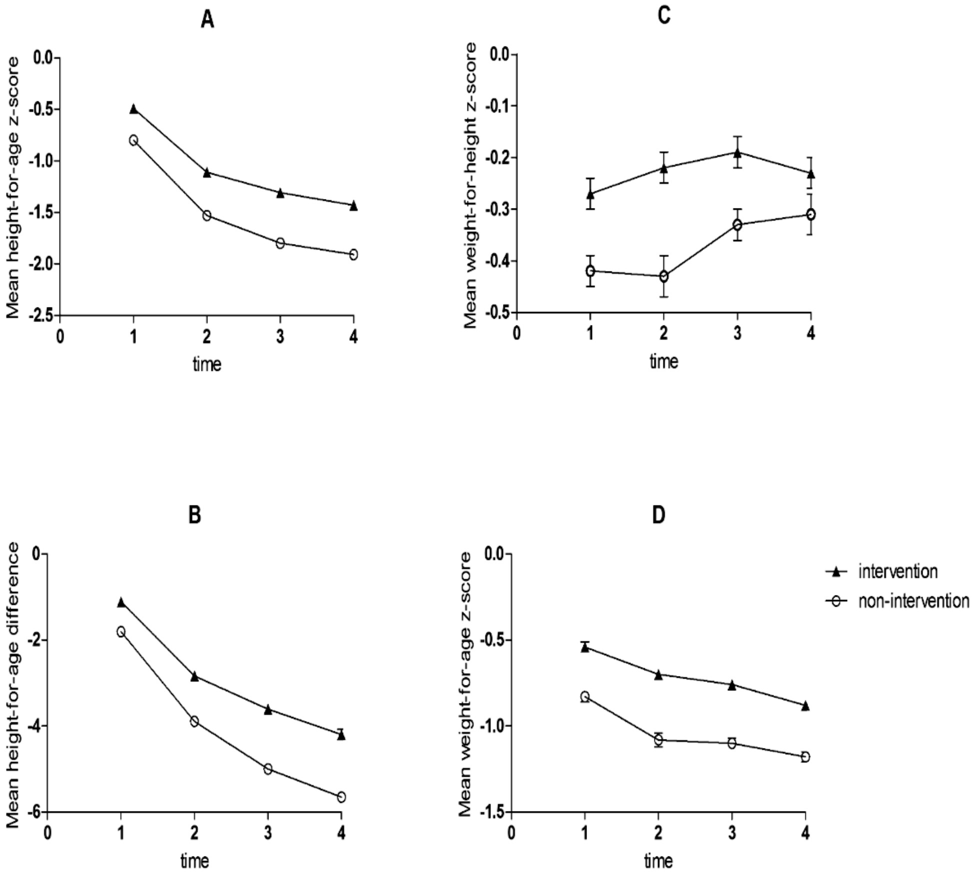

Figure 4. Mean height-for-age z-score (A), height-for-age difference (B), weight-for-height z-score (C) and weight-for-age z-score (D) of intervention during the study period.

Discussion

The findings of this study show that even low iron dose MNPs, provided every other day for eight months, can marginally improve haemoglobin concentrations and result in a remarkable improvement in linear growth when provided in the context of a CF program intervention. However, the low iron dose provided in this supplement may not have been sufficient to increase iron stores. MNPs also resulted in increased diarrhoea and common cold/flu morbidity in the intervention compared to the non-intervention children. However, there were no differences in clinic visits as a proxy for severe disease, and the difference in longitudinal prevalence of diarrhoea became smaller over time, suggesting that the increased morbidity was most likely mild, and indications of a side effect upon introduction of the MNPs.

The 11% non-significant reduction in prevalence of anaemia observed in our study is smaller than the 34% reduction shown in most other MNP studies[5, 26]. In addition, contrary to our findings, most other studies found an effect on iron status as well. Compared to randomized controlled trials, program effectiveness studies in uncontrolled settings often result in lower adherence and subsequently smaller effect sizes[27]. The smaller observed effect on anaemia and no effect on iron status in our study, may have been due to the lower than expected baseline anaemia prevalence in this age-group (36% anaemia observed at baseline in the intervention group vs 73% expected based on the 2012 Ethiopia Demographic and Health Survey among 6-11 month old children). In addition, the relatively low iron dose (6 mg/every 2 days) we provided, may have been just enough for a small increase in haemoglobin levels, but not enough to fill iron stores, while the reduced growth retardation observed in the intervention children in our study suggest that the iron might have been used up by the body for growth being unavailable for storage. Contrary to expectations, we observed higher SF concentrations, a higher increase in SF and a lower prevalence of ID in the non-intervention children, which may be partly explained by the higher presence of acute inflammation as shown by higher CRP and AGP levels at baseline in non-intervention children. While we corrected SF concentrations for inflammation by using the BRINDA approach[22], it is possible that this still did not remove all effects of the acute phase response on SF in this population. Even low levels of inflammation can reduce iron absorption due to elevated Hepcidin concentrations which was one of the explanations for the relatively low efficacy of MNPs on iron status observed in a recent study in Kenya[28].

In our study, children receiving MNP supplementation were 2.3 times as likely as non-intervention children to develop diarrhoea and 2.1 times more likely to develop common cold and flu, but there was no effect on fever. Evidence of increased diarrhoea after MNP supplementation was also observed in a recent meta-analysis[26], although this effect was mainly based on the significant increase in diarrhoea observed in one large study in Pakistan[6], while no increase in morbidity was found in two smaller studies in Nepal[29] and Bangladesh[13]. Our study is comparable in sample size with the study in Pakistan, but we observed a lower overall diarrhoea morbidity in our study population (2.7% and 1.5% in intervention and non-intervention group) compared to the study in Pakistan (6.7 and 5.7%)[29]. Differences in morbidity between geographical locations may have been due to context-specific conditions, whereas in addition the lower iron dose used in our study (6 mg iron every 2 days) as compared to the study in Pakistan (12.5 mg/day) may have contributed to the lower observed morbidity in the intervention group of our study. We did not find a difference in clinic visits between intervention and non-intervention group, which was used as a proxy for severe disease, and the difference in longitudinal prevalence became smaller over time, suggesting that the observed increase in morbidity was likely related to a mild disease, and indications of a side effect upon introduction of the MNPs.

The increase in linear growth and weight gain levels observed in our study are remarkable, and the effect sizes are consistent with a limited number of other studies that show a significant effect of MNP on growth when provided combined with other nutrition or hygiene education interventions[13, 30]. In contrast, MNP interventions alone are not likely to improve growth in most settings[5]. In our study as well, the improved growth cannot be fully attributed to the low dose iron MNP alone as the MNP provision was embedded in a program where local produced CF was distributed. There is a growing level of evidence that combined MNP and IYCF interventions can prompt care-givers to improve complementary feeding practices[31, 32]. The findings of our study suggest that in an area with high levels of childhood malnutrition, such combined MNP and IYCF interventions may have the potential to dramatically reduce stunting levels although the 51% reduction in stunting observed in our study is substantially larger than what has been observed in other settings.

Our study had several limitations. The data collectors were not blinded to the intervention and this may have caused information bias. Although this may have affected the sizes of our effect estimates on morbidity and stunting somewhat, this will not change our overall conclusions. The study had a quasi-experimental design, in which intervention and non-intervention villages were not randomly assigned but purposely selected by the program implementers in close consultation with regional, zonal and district health bureaus. This could have created bias particularly since intervention program villages were selected based on being more vulnerable and more in need of a community-based nutrition intervention. The differences in nutritional status observed at baseline seem to confirm this. Although non-intervention villages were matched with intervention villages based on socio-economic and demographic characteristics, differences between intervention and non-intervention villages in nutritional status and other key characteristics at baseline could therefore not be ruled out, even though we controlled for several of these differences in the analyses. Second, the lower than expected baseline prevalence of anaemia likely affected the power of our study to demonstrate differences in iron status. Thirdly, our analyses in the subsample for the biochemical analyses are further complicated by strong regional differences in, amongst others, dietary habits. While we matched the intervention and non-intervention group at district level resulting in an equal proportion in both regions, the sub-sample for biochemical assessment was selected by going from study village to village, until the required number was obtained. As a result, all children in the non-intervention group were from SNNP whereas most of the children (except 15) in the intervention group were from Oromia. Regional differences in dietary habits and a higher prevalence of food insecurity in Oromia during the time of this study, likely have contributed to the observed difference in iron status among children even at baseline[33]. For example, the major staple food in SNNPR is *kocho*, which is known to be relatively rich in iron[34]. In contrast, the main staple food in Oromia is maize, which is known to be high in phytate affecting iron absorption[34].

Strengths of our study are the implementation of the study in the context of a large-scale program-setting with 8 month duration, the longitudinal design and inclusion of matched-control villages in the design, and the large frequency of data collection involving a large number of children, providing adequate power to study differences in morbidity between groups. Finally, it is the first study providing evidence on the effectiveness of a low iron dose MNP-IYCN program on haemoglobin concentrations and linear growth.

Conclusions

MNPs with low iron dose, when provided combined with other IYCF interventions, marginally improved haemoglobin status, without improving iron stores, and resulted in a remarkable improvement in linear growth in 6-23 month old children, when provided in the context of a CF program intervention. These benefits likely outweigh the relative small increase in risk of diarrhoea, which seemed to be mostly mild in nature and disappeared over time. Nevertheless, programs introducing MNPs in the context of an integrated IYCN intervention, should ensure adequate management, monitoring and control of diarrhoea (with ORS and zinc treatment).

List of abbreviations

AGP: α1-acid glycoprotein; AIC: Akaike Information Criterion; AR1: Auto Regressive Model; BL: Baseline; CSpro: Census and Survey Processing System; CV: Coefficient of variation; CBN: Community Based Nutrition; CF: Complementary Food; CI: Confidence interval; CRP: C-reactive protein; DSMB: Data Safety and Monitoring Board; DID: Difference in difference; EL: Endline; EPHI: Ethiopian Public Health Institute; GLM: General Linear Model; GLMM: Generalized Linear Mixed Models; GPS: Global Positioning System; HAZ: Height-for-Age Z score; Hb: Haemoglobin; IRR: Incidence Rate Ratio; INACG: International Nutritional Anemia Consultative Group; IDA: Iron Deficiency Anaemia; LMM: Linear Mixed Model; MNP: Micronutrient Powder; NRERC: National Research Ethics Review Committee; NI: Nutrition International; SNNPR: South Nations, Nationalities and Peoples Region; SD: Standard Deviation; UNICEF: United Nation Children’s Fund; VC: Variance Components; WAZ: Weight-for-Age Z score; WHZ: Weight-for-Height Z score; WHO: World Health Organization.

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Supplementary Figure, Methods and Table

1. Supplementary Figure

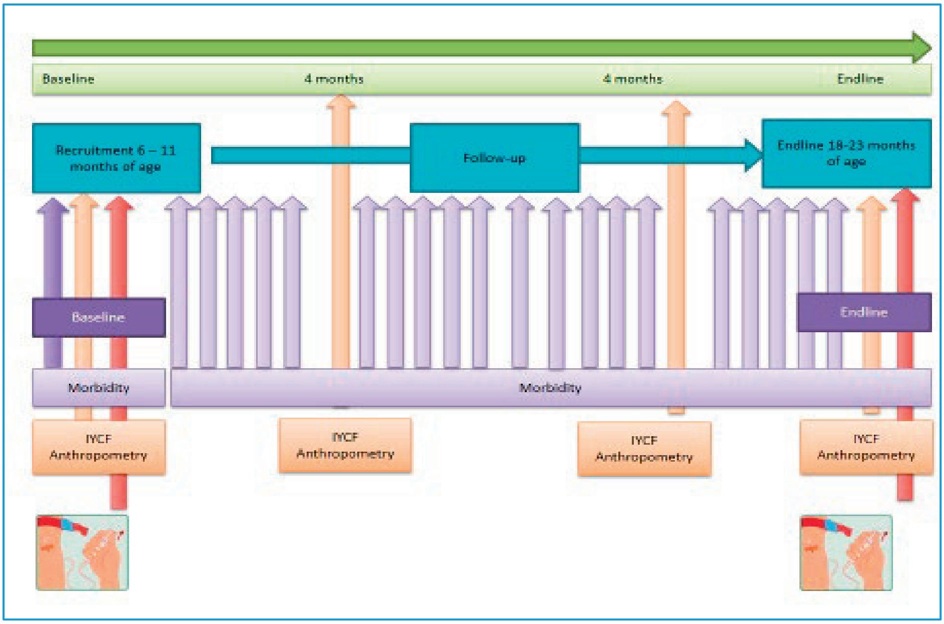

Figure 1. Data collection flow

2. Supplementary methods

Data collection and measurements

The study started in March 2015 and ended in May 2016. During data collection, children who required medical treatment were referred to the nearest health facility, using referral notes and were examined by a Health Officer at the Health Center following standard protocols of the Federal Ministry of Health. We calculated age based on the date of birth (DOB) provided by the mothers/caregivers and if possible using immunization card. The DOB obtained at the baseline was used to calculate the age during the consequent 3 surveys.

Inclusion and exclusion criteria

The data used in this study was from the rural villages of Oromia and South Nations, Nationalities and Peoples (SNNP) regions in Ethiopia. Both regions were selected based on their similar characteristics in food security, child health and nutrition status, and infant feeding practices, which represent the situation of Ethiopian villages. Primary target group of the study were children aged 6-11 months at baseline because the first year of children are considered the most vulnerable. In the main study, 65 eligible children (6-11 months) per cluster/*kebele*; total of 2356 children were included.

Selection criteria for *woreda*, *kebele* and household

*Stage 1: Woreda (*district*) selection*

At the first stage, intervention and non-intervention *woredas* were purposively selected which were 3 intervention *woredas* and 3 non-intervention *woredas* which makes 6 *woredas* per region in total 12.

Inclusion criteria for the *woredas* are shown in the table below.

Inclusion criteria- study *woredas*	
Intervention	**Non-intervention (Control)**
Must have the CBN[1] program running	Must have the CBN program running
Must not have been included in previous pilot	Must not have been included in previous pilot
Will have implementation of grain bank program in the 1st phase	Will not have implementation of grain bank program in coming 2 years

[1] CBN-Community Based Nutrition

*Stage 2: Kebele (*cluster*) selection*

Once the *woredas* were chosen, the *kebeles* within the *woreda* were selected. A list of inclusion criteria for *kebeles* was same as *woredas* (see the table above).

Intervention kebele

A list of all intervention *kebeles* within the *woreda* were obtained from the partnering NGO's, RIPPLE (Research – inspired Policy and Practice Learning in Ethiopia) in the region in collaboration with regional health bureaus. The list of *kebele* were listed in excel and a randomization command(RAND) was performed on the list. If 5 *kebeles* are needed per *woreda*: the first 5 *kebeles* in the list were selected after randomisation.

Control kebele

Lists of all *kebeles* within the control *woreda* were composed. The list of *kebeles* were listed in excel and a randomization command (RAND) was performed on the list. If 5 *kebeles* are needed per *woreda*: the first 5 *kebeles* in the list were selected after randomisation.

Matching

For every intervention *woreda* one non-intervention (control) *woreda* was selected.

Matching was done based on the following characteristics in this order:

1. Zone
2. ENGINE (Empowering New Generations to Improve Nutrition and Economic Opportunities) programme
3. PSNP (productive safety net programme)
4. UNICEF Hot spot (being an emergency *woreda* yes or no)
5. Livelihood which includes socioeconomic status etc

This means the matched intervention and control *woreda* do not have to have all of the above characteristics but they should be equal in it. The order of the characteristics were leading, the 1st being the most important and the 5th being the least important. Matching was then done with the available characteristics.

Stage 3: Household selection

At the third stage, once the identification of sampled clusters or *kebeles* was done, the next step was the selection of households within sampled *kebeles*. Inclusion criteria are shown in table below.

Inclusion criteria- study households	
Intervention	**Non-intervention (Control)**
Must have a child 6-11months	Must have a child 6-11months
Child not having any serious illness that changes his/her food intake	Child not having any illness that changes his/her food intake
Mother/or main caregiver should be present	Mother/or main caregiver should be present
Mother willing to stay in the *kebele* during the study period	Mother willing to stay in the *kebele* during the study period

Obtaining list of children

A list of children and their Date of birth (DOB) and ages were obtained from the Health Extension Worker (HEW) through the *woreda* health office prior to the study. For pre-assessment, the study team went to each region, zone and *woreda* health offices to discuss with officials and to assign a focal person to contact the HEWs and to get the list of children.

With this information, we had purposely selected 10 *woredas* from both regions. We expected, to have 65 children per *kebele* which is 195 children per *woreda*, however, after getting the list of children from *woredas*, we found that there were insufficient number of children in one of the *woreda* called "Sire", so we decided to terminate this *woreda* from study and take more *kebele* from one of the *woredas*, but still considering the same matching *woreda*. Hence, we have taken 3-6 *kebeles* from one *woreda* while matching with their respective *woredas*. So finally we have 9 *woredas* and totally we have 35 *kebeles*.

Prior to screening for admission, all children below 1-year age in the selected villages were listed by Health Extension Workers. The eligibility of potential children was assessed using the criteria as below:

- **Inclusion criteria:**
  1. Living in one of the chosen intervention and non-intervention regions and *kebeles* (Oromia and SNNP)
  2. Age between 6 and 11.99 months old on the recruitment day
  3. MUAC >11.0 cm
  4. WHZ >-3SD Z-score
  5. Had never been provided with other Micronutrient intervention
  6. Free of chronic illness that could affect the child's health
- **Exclusion criteria:**
  1. Children with severe malnutrition condition (Wt /Ht Z-score < -3 SD). Children with this condition were referred for treatment.
  2. Children whose haemoglobin (Hb) concentrations <70 g/L (severe anaemia), these children were referred for treatment.
  3. Presence of a chronic disease and/or chronic use of medications

Laboratory analysis

Biochemical (the concentration of serum ferritin, sTfR , CRP and AGP) analyses (both baseline and endline samples) were done together in the laboratory of Ethiopian Public Health Institute. The laboratory has got certified by Ethiopian National Accreditation Office in accordance with the requirements of ISO 15189:2012[1].

3. Supplementary Table

Pre-intervention morbidity

Table S1. Prevalence and incidence of disease during the pre-intervention period[1]

Variable	Intervention	Non intervention
Longitudinal Prevalence	**N=1148**	**N=1125**
Longitudinal prevalence of diarrhoea Mean (SD)*	6.85(6.68)	4.81(6.24)
Longitudinal prevalence of common cold and flu Mean (SD)*	8.09(8.22)	4.74(6.85)
Longitudinal prevalence of Fever Mean (SD)*	0.17(0.45)	0.21(0.54)
Incidence rate		
Incidence rate of diarrhoea (Per year)	5.45 (4.72)	3.75 (4.11)
Incidence rate of common cold and flu (Per year)	5.73 (5.14)	3.24 (4.12)

[1]Values are mean± SD

Reference

1. ISO. ISO15189 Medical laboratories– Requirements for quality and competence. ISO, Geneva: 2012.

Chapter 5

Determinants of adherence to micronutrient powder use among young children in Ethiopia

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Abstract

Background: In Ethiopia, home fortification of complementary foods with micronutrient powders (MNPs) was introduced as a new, promising approach to improve micronutrient intakes of children. Identifying factors associated with adherence is essential to inform further scale-up of MNPs interventions. The objective of this study was to assess factors associated with adherence and drivers for correct micronutrient powder (MNPs) use over time.

Methods: Mixed methods including a questionnaire survey, semi-structured interviews and focus group discussions.1185 children (6-11 months) received bimonthly 30 MNP sachets for eight months with instruction to consume 15 sachets/month. Adherence to distribution (if child receives ≥ 14 sachets/month) and adherence to instruction (if child receives exactly 15(±1) sachets/month) were assessed monthly by counting used number of sachets. Factors associated with adherence were examined using Generalized Estimating Equations.

Results: Adherence fluctuated over time, with an average of 58% for adherence to distribution and 28% for adherence to instruction. Average MNP consumption was 79% out of the total 120 sachets provided. Factors positively associated with adherence included: ease of use, child liking MNP, support from community and mother's age >25 years. Distance to health post, knowledge of correct use, perceived negative effects and living in Southern Nations, Nationalities and People region were inversely associated with adherence. Free MNP provision, trust in the government and field staff played a big role in successful implementation.

Conclusions: MNPs are promising to be scaled-up, by taking into account factors that positively and negatively determine adherence.

Introduction

In 2016, the World Health Organization published a recommendation about the use of micronutrient powders (MNP) as an effective way of improving the micronutrient status of infants and young children[1]. Home fortification of complementary foods with MNP has several advantages over other fortification methods as described elsewhere[1-4]. Several studies including a meta-analysis of 17 trials conducted so far showed that MNPs are effective in improving micronutrient intakes in women and children (6-59 months of age) and in significantly reducing iron deficiency in developing countries[5-7]. MNP has been successfully used in programs for infants and young children in countries such as Zambia, Sierra Leone, Rwanda, and Madagascar[8].

Findings from the evaluations of these programs suggest that MNP were well accepted by infants and fewer dislikes of the product were reported compared to other supplements[6, 8-10]. Similar findings were also reported in Kenya and Ghana although in Ghana 16 % of the mothers experienced negative effects and problems in giving MNP to their children[9, 11]. Potential barriers identified, among others, were limited knowledge and experience with MNP. Additionally, several studies revealed that mothers preferred a less structured dosing regimen compared to a rigid one[11, 12].

Adherence refers to the extent to which a person follows suggested guidance or advice, in terms of health and medication[13]. It also implies the person's belief and autonomy to freely choose whether or not to practice the recommendation[14, 15]. Numerous documentation from efficacy trials has confirmed the perceived ease of use[13] [14, 15]and high adherence to MNP [16] ranging from 32 to 90% [17]. However, evidence on adherence from large-scale program settings is scarce[18, 19]. In addition, adherence to MNP was measured either at the start or end of the intervention[8, 20] not taking into account changes in adherence over time. Assessing (change in) adherence and its determinants help to understand the (lack of) effectiveness of program interventions[17, 21, 22].

In Ethiopia, MNPs were introduced for the first time in the context of a UNICEF-Nutrition International (NI) led program on local production of complementary foods through rural Grain Banks (hereafter referred to as the Grain Bank program)[23]. As a new program in Ethiopia, assessment of adherence to MNP and analysis of the drivers for correct use are essential to provide evidence-based information for course-correction of program design and implementation, and to further inform scale-up interventions thus eventually contributing to enhanced effectiveness of the program.

Our aim was to explore the determinants of adherence over time, by utilizing the framework of Theory of Planned Behaviour (TPB) summarizing the core elements that predict behaviour of adherence[24, 25] and assess the use of MNP among 6 to 23 months old children in two regions of Ethiopia: Oromia and Southern Nations, Nationalities and Peoples Region (SNNPR), during an eight-month intervention period.

Methods

Study Design

A mixed method design was used comprising quantitative and qualitative methods. Quantitative data were collected using a knowledge, attitude, and practice (KAP) questionnaire. Qualitative data were collected through semi-structured interviews and focus group discussions (FGD).

Study Subjects

Subjects were selected from *woredas* (districts) in Oromia and SNNP regions implementing the Grain Bank program[23, 26].

Both regions were selected based on their large population size and their similar characteristics on food security, child health and nutrition status, and infant feeding practices. This study was part of a larger effectiveness study[27], evaluating the effectiveness of MNPs intervention combined with the Grain Bank program[23].

For this effectiveness study, the five intervention districts implementing the Grain Bank program were selected. From each selected district, 3-4 *kebeles* (clusters) were then purposively chosen, as described elsewhere[27]. From these villages, in total 1185 children were enrolled in the effectiveness study[27]. The current study assessed adherence over time among these 1185 children.

Intervention with Supplementation

The micronutrient powders (MNPs), MixMe®, were manufactured by DSM Nutritional Products in South Africa. Each sachet of MixMe® contained 6 mg of iron in the form of encapsulated ferrous fumarate and 14 other essential vitamins and minerals. The MNPs package was designed specifically for use in Ethiopia[27], labelled in local (Amharic) language and briefly pre-tested among project senior staff. Mothers received 30 sachets every 2 months for every other day consumption (in total 120 MNPs sachets) during the study period (8 months)[27]. Mothers were instructed by the field staff, in the local language, on preparation and correct use of MNPs at the time of distribution and if needed during every data collection time.

Data Collection and Measurements

A KAP questionnaire was used to collect data on adherence and its determinants, administered a month after the start of the intervention and continued monthly during the study for a total of seven rounds. The intervention period was from September 2015 to

April-May 2016. The questionnaire was developed based on the manual of the Home Fortification Technical Advisory Group[28], prepared in English and translated into Amharic language. We used three different versions of the KAP questionnaire for data collection. The first round questionnaire (month 1) had 46 questions but was condensed to 23 questions to reduce the burden on respondents and time for the interview. Quarterly, at months 4 and 7, five questions were added to get more information on the experienced level of social/community support (including husbands, health development army (HDA) and Health Extension Workers (HEWs)) and experience with using MNPs. Since this support was not considered to change frequently, these questions were only asked twice (month 4 and 7). The data collectors were trained intensively on interview techniques and instruments before the start of the study.

Adherence to MNPs Intake

Adherence was measured monthly by counting the empty sachets of MNPs. Mothers were categorized either as adherent or non-adherent based on the minimum number of MNPs they gave to the child per month. Mothers were expected to give a maximum of 15 sachets MNPs per month. Nevertheless, bimonthly MNPs distribution scheme of 30 sachets made it possible for mothers to give >15 sachets and finish all 30 sachets in a month. To account for this condition, adherence was defined according to two definitions:

1. **Adherent to distribution:** if mother gave the child $\geq$ 14 sachets MNPs per month ($\geq$ 95% out of recommended 15 sachets per month). Following this definition, the consumption of 30 sachets per month was also categorized as adherent to distribution.
2. **Adherent to instruction:** if mother gave the child exactly 15($\pm$1) sachets MNPs per month.

Qualitative Data Collection

Semi-structured interviews and FGD were conducted, by trained project staff (TT) including the principal investigator (AS) with field staff, responsible for distribution of MNPs, field supervisors and mothers at two different time points: one and three months after the intervention started.

Table 1. Summary of qualitative data collection

Method	Planned	Conducted
Semi-structured FGD with field staff (n of participants)	5	5(4-6)*
In-depth interview with field staff (n)	17	10
In-depth interview field supervisors (n)*	4	2(2)**
Key Informant Interview with mothers (n)	10	11
Total IDI/KII conducted		25

*A total of 5 FGD were conducted with 4-6 participants; **2 field supervisors were interviewed twice. FGD=Focus Group Discussions. IDI=in-depth interview. KII- key informant interviews

A summary of the qualitative data collected is shown in Table 1. In total 25 interviews (14 in-depth interviews and 11 key informant interviews), and 5 semi-structured FGDs were held and anonymised before analysis. Within the FGD, experience on the program was shared with an emphasis on usage and adherence of MNPs among mothers. For the interviews with mothers, mothers who were at the health post for the monthly follow up were selected randomly, irrespective of adherence or non-adherence. All interviews were recorded and later transcribed in English by two of the project staff and analysed along with notes captured during the interview. The responses were coded and categorized according to the theoretical framework of the Theory of Planned Behaviour (TPB)[29] (see Additional file 2). According to the TPB, behaviour is a conscious effort mediated by intention being a function of three independent determinants namely the attitude towards the behaviour (reflecting the persons judgement of a behaviour); the subjective norm (reflecting social influence); and the degree of perceived behavioural control (reflecting the perceived difficulty of performing the behaviour)[25]. We defined attitude as a perceived belief on the benefit of MNPs as has been mentioned in adherence to medical treatments[13, 24, 30].

Statistical Analysis

Data was entered using CSPro6.0 (Census and Survey Processing System), United States Census Bureau, Suitland, MD, USA. and analyzed in SAS version 9.4, SAS Institute, NC, USA [31] and IBM Corporation, SPSS Statistics version 22, Armonk, NY, USA[32].

Baseline characteristics were presented by percentage for the categorical variables and mean$\pm$SD for the continuous variables. The outcome variable, adherence, was defined by counting the empty sachets of MNPs during monthly visits and, in case the sachets were missing, based on the number of MNPs per month the mother reported to have given to her child. When mothers responded 'don't know' or refused to answer the question asking for the number of sachets of MNPs the child consumed during the last month, the data was considered missing.

Knowledge of correct use of MNPs was measured through 7 questions on dose of the MNPs, type of food that MNPs could be added into, preparation of the food and timing for feeding the MNPs-mixed food to the child. Each correct answer was scored as one. The final score of total correct answers; therefore ranged from 0-7. The responses to questions on attitude (including ease of use and child liking) towards MNPs were dichotomized as 'yes' and 'no'. The multiple responses on the questions about what positive and negative effects mothers perceived after the child consumed MNPs were categorized as perceived no positive effects vs perceived $\geq$1 positive effects and perceived no negative effects vs perceived $\geq$1 negative effects. The questions on mother's confidence and whether mothers felt being supported or not, in providing MNPs to their child, were asked only in months 4 and 7. For these questions, a score of 1 to 5, represented strongly disagree (score 1) to strongly agree (score 5), was given and was analysed as a continuous variable.

The associations between adherence, socio-demographic characteristics, and other determinants were assessed separately for each month using Chi-square tests for categorical variables and Mann Whitney *U* tests for continuous variables. Adherence was analysed separately for adherence to distribution and adherence to instruction. Variables that were significantly associated with adherence were included in the final model using Generalized Estimating Equations (GEE). Two different GEE models were performed to compare associated factors with adherence to distribution and adherence to instruction as dependent variables. The independence among variables analysed in GEE was also checked using multicollinearity test with a cut-off point of variation of inflation (VIF) less than 10. A Cochran Q proportion test was performed to determine if there are differences in the proportion of mothers who perceived the identified benefits of MNPs over the seven months period. A two-sided significance level of $P<0.05$ was applied.

Ethics Approval and Consent to Participate

The study was approved by the Ethiopian National Research Ethics Review Committee (NRERC), Ministry of Science and Technology, reference number 3.10/865/07. Prior to the study, a support letter from the Ethiopian Public Health Institute (EPHI) was provided to each District Health Office and meetings were held with officials and focal persons to inform them about the study and seek verbal consent. Written informed consent was obtained from the mothers/caregivers of all subjects, data collectors, project staff and field staffs by signing or fingerprinting consent form prior to study activity.

Results

The characteristics of study participants per region and age-group are summarized in Table 2. In total 1185 children, 6-11 months of age were screened at baseline, out of which half (50%) were residing in Oromia region. At baseline, the average age of mothers was 25 years and that of children was 8 months. Half of the mothers were illiterate and the majority were married and housewives. About 80% of subjects lived in <60 min walking distance from the local health post.

Table 2. Socio-demographic characteristics of subjects

Characteristics	**n = 1185**
Region (Oromia %)	50.3
Child's age in months , mean ± SD	8.2 ± 1.7
Child's gender (male %)	50.4
Mother's age in years , mean ± SD	25.3 ± 5.6
Illiterate mothers (%)	50.2
Married mothers (%)	94.9
Main occupation of mothers	
Housewife (%)	78.4
Farmer (%)	16.1
Petty trader (%)	3.3
Daily laborer and others (%)	2.2
Walking time from home to health post	
<30 min (%)	377 (41.5)
30-60 min (%)	356 (39.2)
60-90 min (%)	49 (5.4)
>90 min (%)	126 (13.9)
Don't know (%)	277(23.4)

MNPs Consumption and Adherence

The overall MNPs consumption (% of MNPs consumed out of a total of 120 sachets) and the monthly MNPs consumption (% of MNPs consumed out of 15 sachets in a given month) during the intervention is shown in Figure 1. On average, the children consumed 79% of the total MNPs provided during the eight months of intervention. The monthly consumption fluctuated over time with the highest consumption during the second month (129%) and the lowest during the sixth month (77%). Figure 1 also shows that in the first, the second, the fifth and the seventh month, more than 100% of the 15 recommended MNPs servings per month (110%, 129%, 107%, and 119%, respectively) were consumed.

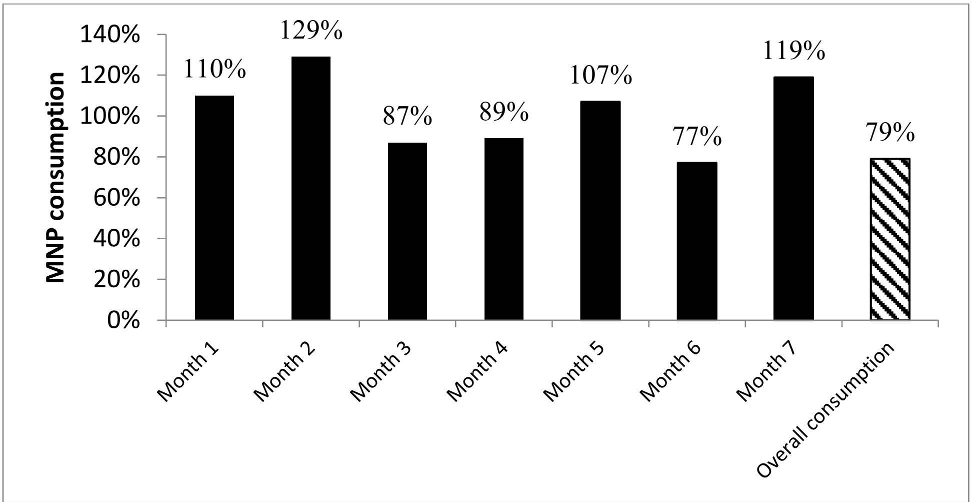

Figure 1. MNPs consumption of children*

*The monthly percentage reflects the percentage of MNPs consumed out of recommended 15 sachets per month. The overall percentage reflects the total MNPs consumed out of total 120 sachets provided during the study.

Adherence of mothers to distribution (if mother gave the child ≥ 14 sachets MNPs per month) and adherence to instruction (if mother gave the child exactly 15(±1) sachets MNPs per month out of recommended 15 sachets) by month (%) during the intervention period is shown in Figure 2.

The average percentage of mothers' adherent to distribution was 58% over the course of the project (Figure 2), with the lowest percentage observed in the sixth month (36%) and the highest in the last month of the intervention (76%). On average only 28% were adherent according to instructions (gave exact 15 (+/- 1) sachets per month) with the lowest adherence to instruction in the second month (11%) and the highest in the seventh month (37%).

Perceived benefits of MNPs

MNPs were quite well accepted by the mothers and liked by children (Table 3). Every month, $\geq$80% of mothers reported that the child liked to consume the MNPs and at least 90% reported that MNPs were easy to use. Almost all mothers (97.3%) perceived at least one positive effect after their children had consumed MNPs. The percentage of mothers experiencing at least one positive effect increased over time from 94.6% to 98.6%. In the first month, 15% of the mothers reported to have experienced negative effects of MNPs and this number decreased in the following months.

Nausea, vomiting, loose stool and black stool were the most frequently reported adverse effects. In general, on average only 4.9% of mothers perceived one or more negative effects of MNPs during the study. With regard to the instructions to use MNPs, most of the mothers (94%) did not report any problems in giving one sachet MNPs every other day to their child.

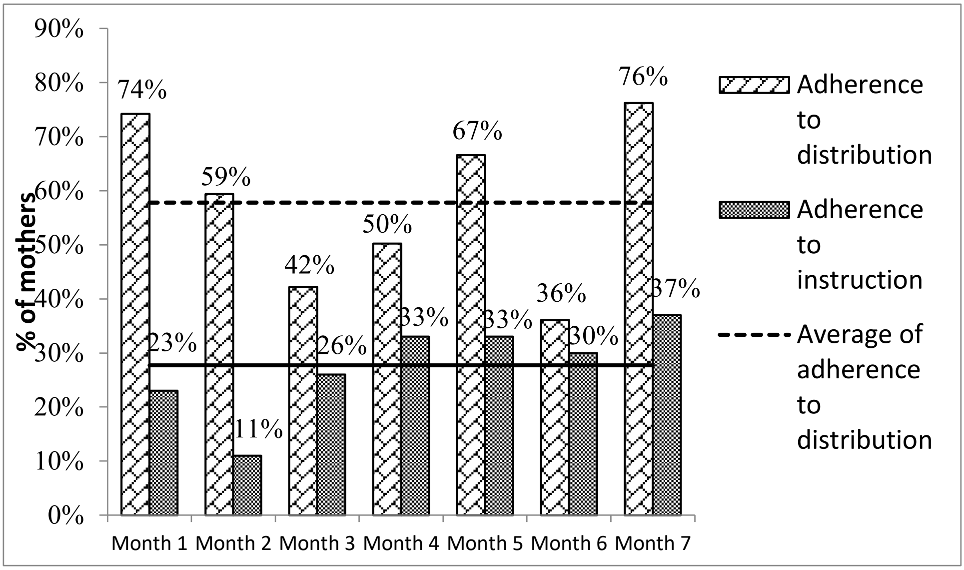

Figure 2. Adherence of mothers in giving MNPs to their child during eight months intervention*

*Adherence to distribution: mother gave minimum 14 sachets per month (95% of recommended 15 sachets per month). Adherence to instruction: mother gave exactly 15(+/-1) sachets MNPs per month. Average adherence was calculated by taking the mean of the monthly percentage.

Table 3. Perceived benefits of MNPs among mothers during the eight-month intervention

Indicator, %*	Month 1 (n=1053)	Month 2 (n=1040)	Month 3 (n=1045)	Month 4 (n=996)	Month 5 (n=1027)	Month 6 (n=1018)	Month 7 (n=1019)	Average
Child liked MNPs	88.4	83.9	86.7	91.8	90.4	88.1	95.0	89.2
MNP was easy to use	89.3	95.3	94.4	98.8	96.6	96.3	96.0	95.2
No problem to give MNP every other day	83.3	94.2	91.9	96.1	96.8	97.4	97.1	93.8
Perceived $\geq$1 positive effects	94.6	96.1	97.2	97.7	98.6	98.6	98.6	97.3
Perceived $\geq$1 negative effects	15.0	11.8	3.1	1.9	0.8	0.6	1.0	4.9

*In all indicators, the percentage over time was significantly different, based on the Cochran Q proportion test, with two-sided significance level p-value <0.05. MNPs=Micronutrient Powders

Determinants of Adherence: Quantitative Measures

The determinants of adherence to distribution and instruction differed slightly per month (see Supplemental Table 1). Determinants of adherence, using summarized data from all 7 monthly rounds of data collection, are presented in Table 4.

Table 4. Determinants of mother's adherence to give MNPs to the child

Variables	Adherence to distribution		Adherence to instruction	
	OR‡ (95% CI)	P-value	OR (95% CI)	P-value
Region (SNNPR)	0.59 (0.52-0.67)	<0.001	0.16 (0.14-0.19)	<0.001
Child's gender (female)	1.01 (0.91-1.12)	0.85	-	-
Mother's age (>25 y)	1.17 (0.76-0.96)	0.006	1.05 (0.89-1.23)	0.575
Mother's educational status (literate)	1.10 (0.98-1.23)	0.114	0.86 (0.73-1.01)	0.068
Marital status (married)	1.04 (0.83-1.31)	0.735	0.87 (0.59-1.27)	0.462
Walking distance from home to health post				
< 30 min (reference)	1.00	-	1.00	-
30-60 min	0.89 (0.79-0.99)	0.040	0.85 (0.72-0.99)	0.049
60-90 min	0.71 (0.55-0.92)	0.009	0.70 (0.51-0.95)	0.024
> 90 min	0.82 (0.70-0.92)	0.027	0.97 (0.78-1.21)	0.787
MNP was easy to use	1.17 (0.90-1.53)	0.228	1.42 (1.01-1.98)	0.042
Had no problem to use MNPs every other day	0.85 (0.68-1.08)	0.239	0.93 (0.73-1.21)	0.160
Knowledge score of correct use of MNPs	0.74 (0.66-0.81)	<0.001	0.96 (0.87-1.08)	0.550
Child liked MNPs	1.57 (1.34-1.84)	<0.001	6.03 (4.48-8.12)	<0.001
Perceived ≥1 positive effects	1.51 (1.04-2.19)	0.031	0.87 (0.50-1.52)	0.627
Perceived ≥1 negative effects	0.73 (0.54-0.99)	0.043	0.73 (0.48-1.11)	0.141
Confident to give MNPs to the child§	0.92 (0.31-2.77)	0.883	2.82 (0.38-21.13)	0.312
Being supported to give MNPs to the child§	1.34 (1.20-1.51)	<0.001	1.17 (1.01-1.36)	0.034

§As these variables were only asked in month 4 and 7, they were analysed using data of month 4 and month 7 only.
‡ Odds Ratios were calculated for every mentioned category of the given determinant, using the alternative values as reference. For instance, the OR for mother's age gives the odds of being adherent for mothers > 25 years, reference to mothers younger or equal than 25 years.

The child liking to consume MNPs was a strong factor positively associated with adherence to distribution (OR=1.57, 95%CI: 1.34-1.84) and to instruction (OR=6.03, 95%CI: 4.48-8.12). Similarly, mothers who felt being supported by their environment were also more adherent (OR=1.34, 95%CI: 1.20-1.51 for adherence to distribution; OR=1.17; 95%CI: 1.01-1.36 for adherence to instruction). About 70% of mothers responded that they were reminded by HDA/Community Health Volunteers and 18% were reminded by health facility staff to collect MNPs (data not shown). The odds of being adherent to instruction was higher among mothers reporting that MNPs were easy to use (OR=1.42, 95%CI=1.01-1.98) and of being adherent to distribution was higher among mothers older than 25 years (OR=1.17, 95%CI=0.76-0.96). Perceiving one or more positive effects of MNPs was positively associated with adherence to distribution (OR=1.51, 95%CI=1.04-2.19) but not with adherence to instruction (OR=0.87, 95%CI=0.50-1.52).

The distance from home to health post was negatively associated with both types of adherence. Mothers who lived with in the shortest distance (<30min) were more adherent than those living further away from the health posts. Knowledge of correct use of MNPs was negatively associated with adherence to distribution (OR=0.74, 95%CI: 0.66-0.81) but not to adherence to instruction (OR=0.96, 95%CI: 0.87-1.08). Mothers became less adherent to distribution (OR=0.73, 95%CI=0.54-0.99) but not to adherence to instruction (OR=0.73, 95%CI=0.48-1.11) when they perceived one or more negative effects after their children consumed MNPs. Living in SNNP region as compared to Oromia was associated with a lower odds for adherence (OR=0.59, 95%CI: 0.52-0.67 for adherence to distribution; OR=0.16, 95%CI: 0.14-0.19 for adherence to instruction).

Positive or Negative Effects Experienced by Mothers: Qualitative Measures

From the qualitative interviews, it appeared that without a clear knowledge about the ingredients and composition of the MNPs, some mothers speculated MNPs was a medicine rather than a food supplement. Some of the mothers who prepared the MNPs in front of their child experienced a rejection of the food by the child. According to them, the powder like nature of the MNPs supported the child's perception that MNPs is a medicine, making him/her reject the food.

In contrast, according to other interviewed mothers, their children liked the MNPs because it made them happy and active. One mother explained:

> *"My child likes the MNPs very much; she even asks me: where is the sugar? She thinks MNPs as a sugar... It makes her happy and active" (Mother).*

Very few mothers experienced negative effects. Of the few negative effects reported, one mother complained about a metallic taste of the food, causing the child to reject it. One of the field staff explained this:

> *"The mother prepared the food with MNPs but waited too long before giving it to the child; the food got a metal taste... That is why the child rejects the food" (Field staff).*

According to the field staff, dislike among mothers in using MNPs was because mothers were getting bored of using MNPs or children started to reject the food with MNPs after some time. One of the field staff said that when the mothers use MNPs repeatedly, the likability and intake would no longer increase but decrease.

Determinants of Adherence: Qualitative Measures

Attitude

All of the interviewed mothers reported experiencing a positive effect on their child after feeding the MNPs. They said that their child has become more active, got a shiny face and a more beautiful skin. When asked how the mothers knew that the child became more active; one mother responded:

> *"There is a great difference between my child and other children of his age, especially in growth and strength… he can pick up anything and throws it away" (Mother).*

Beneficiary effects were mostly mentioned as observational changes. From the interviews, it appeared that mothers who were non-adherent at the start of the study, became adherent when they saw a change in the appearance of their child; and were more motivated to continue using the MNPs. The most frequently mentioned beneficial effect after MNP use was seeing a change in the appearance of their child.

Subjective norm

When asked if the mothers received any social support from their environment, most mothers reported that they did not get any social support with the preparation of MNPs. The mothers also explained that in their culture it was the mother's responsibility to feed the child. However, some felt supported by their husband since ' he' bought the flour and grain to make the porridge. One mother explained:

> *"My husband supports me; he buys the flour I make porridge to mix the MNPs for my child. He says: "the thing you brought from the health post is good for our child, are you giving it regularly? Do not forget to bring it" (Mother).*

Furthermore, it appeared from the interviews that mothers asked for approval from their husband before feeding the MNPs to their child. According to some non-adherent mothers, their husbands did not allow them to come to the health post to collect MNPs. The fathers did not want their child to use the MNPs as they thought it would make the child sicker.

Additionally, some mothers (in their follow up visit or a bi-monthly visit to collect MNPs) gathered together and discussed the program. This made them feel supported and more motivated. According to the field staff, this gathering had several advantages:

> *"When the mothers gather together, they were able to ask each other questions about the MNPs and preparation. They help each other in reminding to give and collect the new MNPs from the health post''. (Field staff)*

External factors

Free provision of MNPs was, according to the field staff, an important factor in adherence and acceptability of the MNPs. The field staff reported that the mothers were used to getting supplements for free from the government. Furthermore, factors such as drought and migration were named to negatively affect adherence. Especially one of the study districts suffered from drought and food shortage during the intervention period. Mothers in this district complained that they were unable to feed their child with MNPs since they had no or limited access to food. Drought led migration was observed in this area. The field staff of one of the study districts described this issue as follows:

> *"Drought is also a big problem. Already a lot of mothers had migrated out of the area because of the drought. It is affecting the study because MNPs needs to be mixed with food, and they do not have enough food. They ask us for additional food to mix the MNPs with". (Field staff)*

Complaints about external circumstances included allocation of time for collecting MNPs and workload for MNPs preparation. Mothers complained that they had no time to prepare the MNP because they were too busy with other responsibilities.

Self-efficacy and trust in the government

Interviewed mothers reported feeling confident in giving the MNP to their child. The main reason mentioned was that the project was performed in cooperation with the government. The use of health posts for the delivery of MNPs gave the mothers trust and made them confident that the product was good for their child's health. One mother explained:

> *"I know you are from the government and you know it is good for him that is why we use it. You brought it and you know it is good. I trust the government; they won't give us anything that is bad for us". (Mother)*

From the interviews, it appeared that mothers themselves were not knowledgeable about the effects of MNPs but trusted the field staff when they were told to use it. This suggested that trust in the government and field staff played a big role in successful implementation of the program. The field staffs reportedly were involved in consulting the mothers on MNP use, correcting them when they made mistakes in preparation or feeding and monitoring the health of their child. All field staff reported having a good relationship with the mothers. The field staff of one study district reported:

> *"They accept things when I say and listen to me… The relationship is very good. They are nice to me and invite me for coffee when I come by their house. They accept things from me and trust me. Since this is a remote area, and they need medical education; so when you go there and tell them your health provision, and say I am here to help you. They are eager to do things like that. They trust me completely". (Field staff)*

Discussion

This study investigated determinants of adherence to MNP use among 6-11 months of age children and their caregivers, living in two regions in Ethiopia. Two definitions of adherence were used based on distribution and dosing instructions. By examining the adherence per month of intervention, it was found that adherence fluctuated over time, with an average of 58% for adherence to distribution and 28% for adherence to instruction. Following the instructions of one sachet every other day, mothers were expected not to give more than 15 sachets of MNPs per month to their children. However, the bimonthly distribution scheme was thought to lead to the observed fluctuations in adherence over time and low adherence to distribution on average. These issues with adherence could have been avoided if MNPs were distributed more frequently, e.g. on a monthly basis. Moreover, as mothers were instructed not to give MNPs when their child was sick, 8% of the mothers reported suspending MNPs during the sick days. After the illness, mothers had also been taught to compensate for the missing days by providing MNPs daily for some time; which turned out to be a difficult instruction to follow. In addition, inconsistency between on-pack, "do not give more than one sachet MNPs per day", and oral dosing instructions "give MNP every other day", may have caused mothers to use more than the instructed 15 sachets per month, resulting in the low observed adherence and confirms the need for a proper pre-test of the packaging. The issue with inappropriate packaging was previously also experienced in Kenya which, in part, caused a nearly 70% drop in MNPs uptake from 99% to 30% during 17 months of provision[33]. In addition, a recent review of the literature on factors affecting adherence to MNP programs identified issues with administration regimen, related to caregivers' capacity to remember to give MNPs, as an important program design feature affecting adherence[34].

Overall, we found low adherence to MNPs which is consistent with the findings of other studies. Low adherence were previously reported in Peru (MNPs consumption, every other day for 6 months) and in Aboriginal children in Canada (with consumption of sprinkles containing 30 mg Fe/day for 6 months) which was explained by disliking the taste of the MNPs (49%) and forgetting to give the MNPs to the child (60%) respectively[35, 36]. Similar to the study in Canada, we also observed on average 5% of mothers forgetting to give MNP (data not shown) according to instructions.

The study showed that acceptability of MNPs and total consumption out of 120 sachets provided overtime was good. This is consistent with other studies published[9, 10, 22, 37]. In addition, the WHO has recommended consumption of 90 sachets within a timeframe of 6 months for the same age group to improve micronutrients intakes[1]. In contrast, a meta-analysis of previous studies in other developing countries reported that the consumption of MNPs has generally been >83%[38]. However, most of these studies were trials which were conducted in controlled settings which can explain their slightly higher consumption as compared to our intervention embedded in a program setting.

Like other studies[33, 39-41], every month more than 90% of mothers in this study, reported at least one positive effect such as increased health, activity, strength, appetite, growth, energy, more beautiful skin and shiny face of the children. The "child liking MNP" was a strong factor positively associated with adherence to distribution and adherence to instruction, similar to the findings in Nepal[42]. Following the Theory of Planned Behaviour (TPB) [24], mothers would have a more positive attitude towards MNPs and therefore an increased intention to use MNPs when they observed their child liking the MNPs. Similar to our findings, a recent review paper of literature on factors affecting adherence also concluded that caregivers' perception of positive changes, caregivers' perceived child acceptance of food with MNPs and forgetfulness, were the most important factors affecting adherence[34].

In addition, our study also found that social/community support was positively associated with adherence. Mothers who received support from their surrounding such as husbands were more likely to adhere than those who did not. Other studies also showed approval of husbands having a significant role for decision making[43, 44]. In the TPB, social support constructs a subjective norm factor which refers to the perceived social pressure to or not perform the required behaviour [24]. Health development army, health extension workers, and husbands were the most frequently reported persons who gave support to mothers during the intervention by reminding them to go to health posts and collect MNPs every two months. Our findings of the positive association of social support to adherence were also in line with the study in Mexican children[45] and the systematic review of iron supplementation[46]. This suggests that family members have a significant role in acceptability and use of MNPs.

The factor of perceiving one or more positive effects of MNPs influenced adherence differently depending on the definition of adherence used. It increased the adherence to distribution but decreased the adherence to instruction. A plausible explanation for this finding might be that when mothers had a positive attitude to MNPs they would give MNPs to the child more frequently, and subsequently, the consumption would be more than 15 sachets per month. Adherence to distribution was lower when negative effects were perceived, despite the fact that only 4.9% of mothers reported any negative effects.

An inverse association was found between knowledge and adherence, though almost all mothers (>95%) answered correctly all questions about how to use MNPs. This implies that level of knowledge may not simply relate to performing a behaviour, and in the present study, mothers might not make knowledge-based decisions for performing behaviour of adherence. It is generally known that knowledge has been consistently non-influential in predicting behaviour performance[25, 47].

The current study showed that mothers who were living in SNNP region were less adherent than mothers in Oromia region. This may be due to the contextual factors that may differ from region to region. Those factors include a commitment from the local staff, local programs, or social and cultural differences[48] which should be considered when planning a tailor-made MNP program. Therefore, it is important to locally tailor the MNP implementation programs to address the regional variation by enforcing additional inputs such as preparing context- specific behaviour change intervention materials and providing regional level training.

This study has some limitations that need to be acknowledged. First, since there were no data from a control group, it could not be confirmed whether the found effects were related to MNPs alone. A second limitation of our study is that the analysis did not take into account factors associated with the health workers which may have impacted mothers' adherence to the intervention[33, 49, 50]. In particular, information on the level of education, job experience and satisfaction, knowledge, skills, and perception of health workers on MNPs, their expectation from the program and the level of support health workers provide to mothers was not measured. Another limitation is the use of self-reported adherence. It is important to realize that mothers might give different responses because they report to their data collector instead of to an independent interviewer. In addition, the fact that interviewers asked the same questions every month, might have led to social desirability bias[51]and an overestimation of adherence[30], however, several repeated questions were asked to check the reliability of the responses.

An important strength of our study is that it was conducted within the context of a large-scale program setting involving a large number of subjects thus portraying a "real-life" situation. Furthermore, adherence and determinants were assessed every month which allowed for comparison of adherence and associated factors over time. This enabled us to forward recommendations which should be taken into account while designing strategies in the intervention program. Finally, it is the first evidence-based data on adherence to an MNP program in Ethiopia to use as a reference.

Recommendations for future programs and research include aligning the instruction on the packaging with the distribution and consumption schedule. Monthly distribution helps to better monitor the consumption and also reach the desired program adherence. The benefit of frequent distribution has been experienced in previous studies[9, 16] in Haiti (96%)[52] and Lao (100%) with a monthly and weekly distribution respectively[53]. A frequent distribution is believed to encourage more interactions between mothers and health workers[42]. On the other hand, since increasing distribution frequency might increase program cost including mother's time, a high adherence can also possibly be achieved by applying a less rigid instruction and definition of adherence. For example, to give 60 sachets of MNPs in a flexible administration over 3 (or 4) months or 90 sachets in 6 months as per WHO 2016 guideline[1]; with the instruction to not exceed consumption of one sachet per day. Such a flexible scheme can be an option especially when MNPs are included in longer-term, large-scale programs where intensive supervision cannot be guaranteed. Moreover, giving autonomy to mothers to choose when and how often to use MNPs would make it easier for them to adapt to and thus adhere to the programme[54, 55].

Since social support was a significant determinant of adherence among mothers, empowering husbands and health workers (HDA and HEW) to be more involved in the program seems essential[35, 56]. However, this may increase the workload especially for HEW, thus consideration should be taken into account to adjust this recommendation with the existing capacity and health system in the country and/or by using other delivery channels that may be more relevant for husbands or male influencers, such as agricultural workers[57].

Conclusion

The adherence of mothers in giving MNPs fluctuated over time during an eight months intervention, with a low overall adherence: 58% for adherence to distribution and 28% for adherence to instruction. The main reasons for the low adherence were considered to be a less frequent distribution scheme and inconsistent instructions. Nevertheless, average consumption of 79% of received MNPs was observed and the acceptability was good both among mothers and children. These findings suggest that future programs scaling up MNPs interventions should take into account factors associated with adherence in their program design, for instance by adapting dosing regimen and instructions and by including the social environment in the behavioural change campaigns.

List of Abbreviations

CSpro: Census and Survey Processing System; CBN: Community Based Nutrition; EPHI: Ethiopian Public Health Institute; GEE: Generalized Estimating Equations; Hb: Haemoglobin; HDA: Health Development Army; HEW: Health Extension Workers; KAP: Knowledge, Attitude and Practice; MI: Micronutrient Initiative; MNPs: Micronutrient Powders; NRERC: National Research Ethics Review Committee; SNNPR: South Nations, Nationalities and Peoples Region; TPB: Theory of Planned Behaviour; UNICEF: United Nation Children's Fund; WHO: World Health Organization; VIF: Variation of Inflation

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Supplemental Tables and Figure

Supplemental Table 1. Association between adherence to distribution with socio demographics characteristics and other determinants analysed from the monthly data*

N adherent / non-adherent§	Month 1		Month 2		Month 3		Month 4		Month 5		Month 6		Month 7	
	746/260		615/421		443/592		495/492		684/341		365/646		760/237	
Variables	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P
Region		0.880		<0.001		0.001		<0.001		0.001		<0.001		0.002
Oromia	44.8/45.4		39.3/56.8		55.7/44.9		57.7/33.9		51.6/40.5		78.0/30.3		43.1/54.9	
SNNPR	55.2/54.7		60.7/43.2		44.3/55.1		42.3/66.1		48.4/59.5		22/69.7		56.9/45.1	
Child's age◇		0.265		0.066		0.452		0.421		0.438		0.558		0.341
<8 months	43.8/48.2		49.0/42.2		46.9/44.4		46.6/43.9		45.7/42.9		46.1/44.0		46.7/42.9	
>8 months	56.2/51.8		51.0/57.6		53.1/55.6		53.4/56.1		54.3/57.1		53.9/56.0		53.3/57.1	
Child's gender		0.433		0.046		0.666		0.566		0.047		0.690		0.829
Male	51.3/48.5		47.1/53.4		50.0/51.4		51.6/49.8		47.7/54.3		50.7/49.0		50.3/51.1	
Female	48.7/51.5		52.9/46.6		50.0/48.6		48.4/50.2		52.4/45.8		49.3/51.0		49.7/48.9	
Mother's age		0.099		<0.001		0.053		<0.001		0.544		0.028		0.001
<25 years	42.8/44.0		37.9/50.6		40.8/46.8		37.6/49.0		43.8/41.8		39.1/46.3		45.8/33.5	
>25 years	57.2/56.0		62.1/49.4		59.2/53.2		62.4/51.0		56.2/58.2		60.9/53.7		54.2/66.5	
Mother's education level		0.081		0.003		0.249		<0.001		0.825		<0.001		0.001
Illiterate	50.9/44.6		46.2/55.6		49.1/50.9		56.9/43.5		49.7/50.4		62.5/44.0		46.3/58.8	
Literate	49.1/55.4		53.9/44.4		52.7/47.3		43.1/56.5		50.3/49.6		37.5/56.0		53.7/41.2	
Marital status		0.418		0.605		0.341		0.005		0.117		0.377		0.122
Unmarried	5.1/3.9		4.8/5.5		4.3/5.6		6.7/2.9		4.0/6.2		5.2/4.0		4.0/6.9	
Married	94.9/96.1		95.3/94.5		95.8/94.4		93.3/97.1		96.0/93.8		94.8/96.0		96.0/93.1	
Walking distance from home to health post		0.397		<0.001		0.496		0.014		<.0.001		0.499		0.336
<30 min	40.2/46.1		45.6/28.2		43.8/38.8		37.7/46.0		45.2/30.0		36.5/41.2		42.4/35.2	
30-60 min	41.0/35.3		38.8/42.6		37.0/40.3		38.2/37.4		35.1/47.7		41.0/40.1		37.6/44.1	
60-90 min	5.4/5.8		4.3/6.6		5.1/6.4		5.2/5.2		4.2/7.8		5.9/5.0		5.3/5.0	
>90 min	13.3/12.9		11.3/22.5		14.1/14.6		18.8/11.4		15.5/14.5		16.6/13.7		14.8/15.6	

*Chi-square tests were performed for categorical variables and Mann Whitney tests for continuous variables. Two-sided significance level of P-value <0.05 was applied. §Sample size might vary due to missing data. ◇This variable is not associated with adherence in any months so it was not included in the GEE model.

Chapter 5

Supplemental Table 1. (continued)

	Month 1		Month 2		Month 3		Month 4		Month 5		Month 6		Month 7	
N adherent/non-adherent§	746/260		615/421		443/592		495/492		684/341		365/646		760/237	
Variables	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P
MNP was easy to use (yes)	91.2/89.4	0.391	94.8/96.1	0.314	96.2/94.4	0.195	98.9/99.0	0.569	98.8/92.1	<0.001	95.1/96.9	0.141	95.4/97.5	0.160
Had problem to use every other day		<0.001		0.011		0.742		<0.001		0.009		<0.001		0.402
(no)	11.7/22.7		7.3/3.6		7.2/7.8		6.7/1.2		4.4/1.2		6.0/0.8		3.2/1.2	
Knowledge score of correct use of MNP (median)	6/6	<0.001	7/7	<0.001	7/7	0.004	7/7	0.021	7/7	0.654	7/7	<0.001	7/7	<0.001
Child liked MNP (yes)	91.8/77.1	<0.001	77.0/94.1	<0.001	84.8/88.3	0.099	97.0/86.7	<0.001	90.2/90.6	0.834	94.5/84.4	<0.001	94.3/96.6	0.164
Perceived >1 positive effects		<0.001		0.664		0.005		0.836		0.181		0.553		0.982
(yes)	97.2/90.4		96.7/95.7		98.9/95.9		97.8/98.0		99.0/97.9		99.2/98.6		99.1/97.5	
Perceived >1 negative effects		<0.001		<0.001		0.007		0.989		0.251		0.197		0.709
No	87.7/78.8		93.1/81.0		98.4/96.6		98.2/98.2		99.6/98.5		98.9/99.7		99.1/98.7	
Confident to give MNP to the child		0.002	*	-	-	-		0.287	-	-	-	-		0.012
Yes	96.9/92.3						98.8/99.6						99.1/96.6	
Being supported to give MNP to the child (median)	-	-	-	-	-	-	4/3	<0.001	-	-	-	-	3/3	0.001

*This variable was not asked in the KAP questionnaire in the corresponding months

Supplemental Table 2. Association between adherence to instruction with socio demographics characteristics and other determinants analysed from the monthly data*

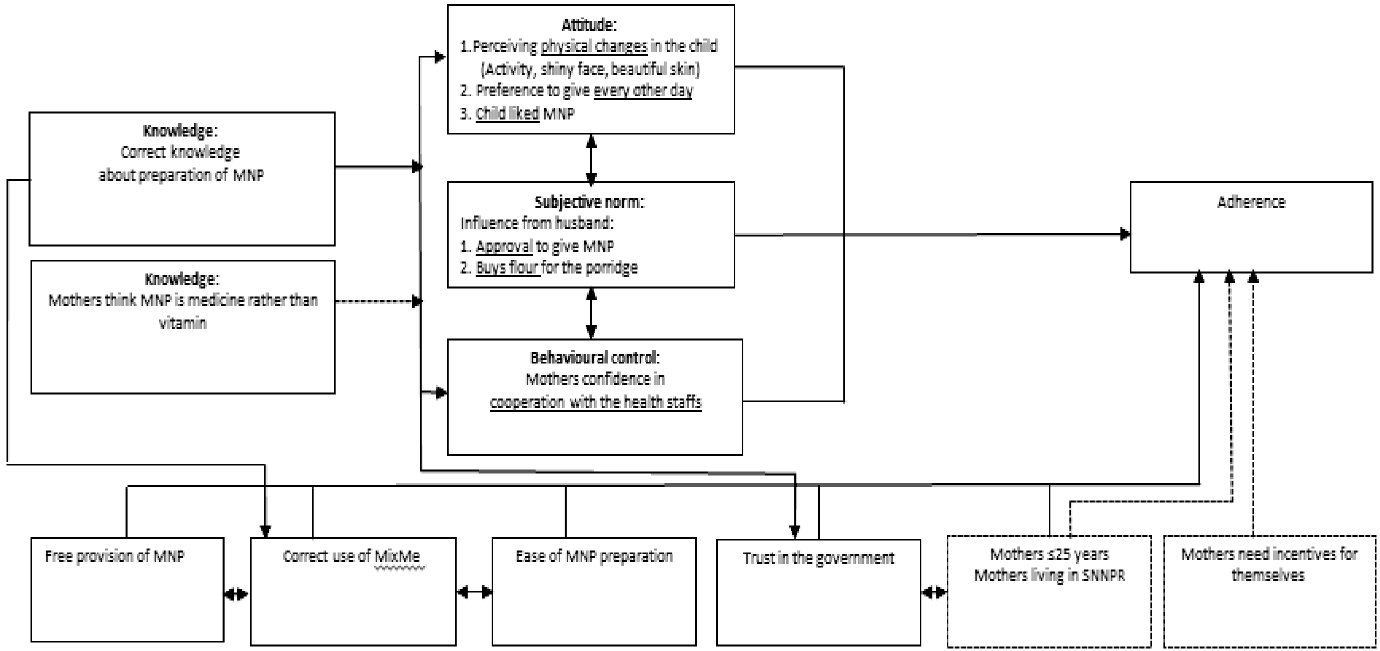
N adherent / non-adherent§	Month 1		Month 2		Month 3		Month 4		Month 5		Month 6		Month 7	
	236/770		117/919		267/768		322/665		337/688		306/705		371/626	
Variables	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P	% adherent/non-adherent	P
Region		0.427		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001
Oromia	47.2/44.3		89.7/40.9		63.3/44/7		87.2/25.8		81.3/31.6		78.6/33.9		77.8/26.9	
Child's age◇		0567		0.264		0.745		0.665		0.485		0.438		0.115
<8 months	46.7/44.4		40.8/46.8		46.4/45.2		46.3/44.7		43.1/45.5		46.7/43.9		49.2/43.7	
>8 months	53.3/55.6		59.2/53.2		53.6/54.8		53.7/55.3		56.9/54.5		53.3/56.1		50.8/56.3	
Child's gender◇		0.571		0.718		0.515		0.815		0.948		0.376		0.106
Male	48.9/51.0		51.3/49.5		49.1/51.4		51.2/50.5		50.0/49.8		52.0/49.0		53.8/48.5	
Mother's age		0.407		0.783		0.006		0.011		0.085		0.056		0.904
<25 years	40.8/43.8		41.9/43.2		50.6/40.9		49.1/40.5		39.3/45.0		39.1/45.6		39.5/44.9	
>25 years	43.8/56.2		58.1/56.8		49.4/59.1		50.9/59.5		60.7/55.0		60.9/54.4		60.5/55.1	
Mother's education status		0.278		0.008		0.057		0.001		<0.001		<0.001		<0.001
Illiterate	52.4/48.3		61.5/48.5		56.2/49.4		57.8/46.5		65.5/42.4		64.1/44.8		58.6/43.6	
Literate	47.6/51.7		38.5/51.5		43.8/50.6		42.2/53.5		34.5/57.6		35.9/55.2		41.4/56.4	
Marital status		0.528		0.022		0.876		0.033		0.482		0.142		0.020
Unmarried	5.6/4.6		9.4/4.5		4.9/5.1		6.9/3.8		5.4/4.4		5.9/3.8		7.0/3.7	
Married	94.4/95.4		90.6/95.5		95.1/94.9		93.1/96.2		94.6/95.6		94.1/96.2		93.0/96.3	

*Chi-square tests were performed for categorical variables and Mann Whitney tests for continuous variables. Two-sided significance level of P-value <0.05 was applied. §Sample size might vary due to missing data. ◇This variable is not associated with adherence in any months so it was not included in the GEE model

Supplemental Table 2. *(continued)*

	Month 1		Month 2		Month 3		Month 4		Month 5		Month 6		Month 7	
N adherent/non-adherent	236/770		117/919		267/768		322/665		337/688		306/705		371/626	
Variables	% adherent/ non-adherent	P	% adherent/ non-adherent	P	% adherent/ non-adherent	P	% adherent/ non-adherent	P	% adherent/ non-adherent	P	% adherent/ non-adherent	P	% adherent/ non-adherent	P
Walking distance from home to health post		<0.001		0.022		0.105		0.001		<0.001		0.122		0.017
<30 min	53.2/38.1		40.0/38.7		35.7/42.7		36.1/44.3		33.1/43.0		41.9/38.8		40.6/40.9	
30-60 min	36.2/40.5		28.9/41.7		39.0/38.8		34.7/39.0		35.9/40.9		34.2/42.7		33.7/41.8	
60-90 min	5.0/5.7		5.6/5.1		6.2/5.7		5.9/4.9		6.0/5.2		5.9/5.1		5.8/4.9	
>90 min	5.5/15.7		25.6/14.5		19.0/12.8		23.3/11.8		25.1/10.8		18.0/13.4		19.9/12.4	
MNP was easy to use (yes)	87.4/91.7	0.050	97.4/95.1	0.264	95.1/95.2	0.976	98.1/99.1	0.196	99.1/95.3	0.002	98.4/95.3	0.019	95.7/96.1	0.722
Had problem to use every other day (no)	16.6/13/9	0.300	8.5/5.4	0.175	8.2/7.3	0.613	10.2/0.9	<0.001	7.4/1.2	<0.001	2.0/3.0	0.356	3.5/2/6	0.424
Knowledge score of correct use of MNP (median)	7/6	<0.001	7/7	0.001	7/7	<0.001	7/7	<0.001	7/7	<0.001	7/7	<0.001	7/7	<.0.001
Child liked MNP (yes)	93.2/86.4	0.006	86.3/83.7	0.459	96.6/83.4	<0.001	98.1/88.8	<0.001	97.6/86.8	<0.001	2.9/15.9	<0.001	94.6/95.2	0.669
Perceived ≥1 positive effects		0.524		0.801		0.001		0.180		0.568		0.239		1.00
Yes	96.2/95.2		95.7/96.1		100/96.2		98.8/97.4		99.1/98.4		99.0/98.7		96.7/98.7	
Perceived ≥1 negative effects		0.754		<0.001		0.186		0.145		0.284		0.374		0.101
No	86.0/85.2		76.9/89.7		98.5/97.0		99.1/97.7		99.7/99.0		99.0/99.6		99.7/98.6	
Confident to give MNP to the child		0.447	*	-	-	-		0.768	-	-	-	-		0.012
Yes	94.8/96.0						99.1/99.2						99.1/96.6	
Being supported to give MNP to the child (median)	-	-	-	-	-	-	2/3	<0.001	-	-	-	-	3/4	<0.001

*This variable was not asked in the KAP questionnaire in the corresponding months



Supplemental Figure 1
Theoretical frame work describing factors affecting adherence (use and continues use of MNP).
The lines reflect a positive correlation with adherence and the dotted line reflects a negative correlation with adherence.

Chapter 5

Chapter 6

General discussion

Ensuring optimal infant and young child feeding (IYCF) practices has been identified as one of the most effective public health interventions to improve child survival in developing countries[1]. In Ethiopia, the fact that child undernutrition is a critical public health problem with high rates of stunting due mainly to poor complementary feeding practices[2] highlights the need to improve our understanding of IYCF. The overall aim of this thesis was to optimize young child complementary feeding by analysing the effectiveness, acceptability, and potential risks of micronutrient powders (MNPs). To achieve this aim, four studies were carried out, focusing on analysing and optimizing the diets of infants and young children and studying the effects of an integrated nutrition intervention using MNPs in Ethiopia.

The studies reported were carried out in the framework of the Ethiopian community-based nutrition (CBN) programme and the embedded United Nations International Children's Emergency Fund (UNICEF)–Nutrition International-supported local complementary food (CF) production programme (the Grain Bank programme) to improve the quality of CF and IYCF practices in semi-urban and rural areas in four regions (Amhara, Oromia, Tigray, and Southern Nations, Nationalities, and Peoples (SNNP))[3]. The studies were conducted in rural areas in two of the four programme regions, Oromia and SNNP. As far as we know, this was the first study on the effectiveness of low-iron-dose MNPs in a scaled-up programme context with limited control over intake and compliance. Evaluating the drivers of correct use, potential risks, and adherence to MNPs in such a programme setting is pertinent to develop evidence-based information for programme design and implementation.

In this chapter, the main findings of this thesis are first summarized and then methodological considerations are reflected upon. Subsequently, the contribution of this thesis to understanding young child nutrition in Ethiopia and the effectiveness of, adherence to, and potential risks of introducing, MNPs are further discussed.

Conclusions are drawn from the findings, followed by implications for public health and recommendations for further research.

Main findings

The main findings of the thesis are summarized in Table 1. **Chapter 2** describes the gender differences in determinants of nutritional status and the association of IYCF practices, dietary intake, and maternal and household characteristics with stunting and wasting. Using cross-sectional data for infants living in Oromia and SNNP, we showed that stunting and wasting were highly prevalent in the regions, more in boys than in girls. Untimely initiation of breastfeeding, non-exclusive breastfeeding, region of residence, and low maternal education are significant predictors of stunting in boys. Untimely introduction to CF and low consumption of legumes/nuts are significant predictors of stunting in both boys and girls, and low egg consumption only in girls. Although some predictors were statistically significant only in boys and not in girls, there was little indication of significant effect modification by gender. Only the association between stunting and initiation of breast feeding showed a large difference between boys and girls: it was a significant risk factor for stunting in boys, but clearly not in girls.

Table 1. Summary of the main findings of each study conducted in Ethiopia covered in the thesis

Objectives	Main results
Chapter 2 *Type:* Cross-sectional *Population:* Infants aged 6–11 months (n=2036) in Oromia and SNNP	
• Assess gender differences in determinants of nutritional status	• The prevalence of stunting and wasting was significantly higher among boys (18.7 and 7.9%) compared to girls (10.7 and 5.4%), respectively • Untimely initiation of breastfeeding, non-EBF, region of residence, and low maternal education were significant predictors of stunting in boys, but not in girls • Untimely introduction to CF and low consumption of legumes/nuts were significant predictors of stunting in both sexes, and low egg consumption only in girls • Region of residence and age of the mother were significant predictors of wasting, with no differences between boys and girls • There was an indication of an interaction between early initiation of breastfeeding and gender (*p*=0.12), suggesting that the association between initiation of breastfeeding and stunting was different for boys and girls
Chapter 3 *Type:* Cross-sectional *Population:* Children aged 6–23 months (n=2504) in Tigray, Amhara, Oromia, and SNNP	
• Determine nutrient adequacy of young children's diet • Identify best possible strategies to improve nutrient adequacy	• The sets of FBDRs were considerably different for the four regions • Optimized local diets did not provide adequate zinc in all regions and age groups; iron for infants <12 months of age in all regions; and calcium, niacin, thiamine, folate, vitamins B_{12} and B_6 in some regions and age groups • A combination of regional FBDRs with daily MNPs for 6–11-month olds and every other day for 12–23-month olds closed the identified nutrient gaps without leading to a substantial increase in risk of excess intake of iron and zinc
Chapter 4 *Type:* Matched control-quasi experimental MNP intervention (every other day for 8 mo) *Population:* Children aged 6–11 months (n=2309) in Oromia and SNNP	
• Assess the effectiveness and risks of an integrated programme with low-iron-dose (6 mg/serving) MNPs	• Reduction in anaemia prevalence (from 35.7 to 24.8%) in intervention children (but without improvement in iron stores) compared to a stable prevalence in non-intervention children (from 27.1 to 29.5%) • Intervention children were 2.31 times more likely to have diarrhoea and 2.08 times more likely to have common colds and flu than non-intervention children, but these increases disappeared towards the end of the intervention • A higher average increase in height (0.82cm) and weight (0.11kg) was observed in intervention compared to non-intervention children
Chapter 5 *Type:* Mixed methods (quantitative and qualitative) *Population:* Children aged 6–11 months (n=1185) in Oromia and SNNP	
• Analyse the drivers of correct use of, and adherence to, MNPs among mothers of young children	• Average MNP consumption over the intervention period was 79% of the total 120 sachets provided • Adherence fluctuated over time, with an average of 58% for adherence to distribution and 28% for adherence to instruction • Distance to health post, knowledge of correct use, perceived negative effects, and residing in SNNP were negatively associated with adherence

Abbreviations: CF: Complementary food; EBF: Exclusive breastfeeding; FBDR: Food-based dietary recommendation; IYCF: Infant and young child feeding; MNPs: Micronutrient powders; NFCS: National Food Consumption Survey

Analysis of data from the 2011 Ethiopian National Food Consumption Survey (NFCS) showed that dietary habits differ greatly across the various geographical regions in Ethiopia (**Chapter 3)**. We formulated sets of region-specific and age-appropriate food-based dietary recommendations (FBDRs) to optimize nutrient adequacy, but results show that even if the developed FBDRs were fully adopted, intakes of zinc (in all age groups and regions), iron (for infants <12 months of age in all regions), calcium, niacin, thiamine, folate, and vitamins B_{12}, and B_6 (in some regions and age groups, but not in all) might remain suboptimal, indicating the need for additional interventions. The study further indicated that the best option to achieve nutrient adequacy is a combination of regional FBDRs and home fortification with daily MNPs for children 6–12 months of age and every other day for children 12–23 months of age. It was confirmed that these dosages would not lead to substantial excessive intake of iron and zinc for either age group.

In **Chapter 4**, the effectiveness, benefits, and potential risks of an integrated complementary feeding intervention providing low-iron-dose (6 mg/serving) MNPs (every alternate day) for 8 months are addressed. We found that haemoglobin concentration increased in the intervention group and slightly decreased in the non-intervention group, with no change in iron stores. Intervention children had a higher mean height-for-age z score (HAZ) and 51% reduced odds of being stunted compared to non-intervention children. The prevalence of stunting and underweight increased in both the intervention and the non-intervention group, but to a lesser extent in the intervention group. The change in wasting during the intervention period was not different between groups. We observed an increased incidence of diarrhoea and the common cold/flu in the intervention group compared to the non-intervention group, but these increases disappeared towards the end of the intervention.

Chapter 5 describes the use of MNPs and the determinants of adherence over time, utilizing the Theory of Planned Behaviour (TPB) framework, which outlines the core elements that predict adherence behaviour[4]. Adherence was low and fluctuated over time, with an average of 58% for adherence to distribution (if mother gave the child $\geq$ 14 sachets MNPs per month) and 28% for adherence to instruction (if mother gave the child exactly 15($\pm$1) sachets MNPs per month). MNPs were quite well accepted by the mothers and liked by children. We observed that most of the mothers did not report any problems with regard to the instruction to give one sachet MNPs every other day. However, we noted that adherence fluctuated over time, probably due to the inconsistency in the bimonthly distribution scheme and monthly follow-up. In addition, inconsistency between the on-pack instruction "do not give more than one sachet MNPs per day" and the oral dosing instruction "give MNPs every other day" might have caused the observed low adherence. Factors positively associated with adherence included: ease of use, child liking MNPs, support from community, and mother's age >25 years.

Methodological considerations

In this section, the internal validity of the studies in this thesis is addressed, in relation to the reliability or accuracy of the study results[5]. Issues discussed include *study design*, *selection bias*, *information bias*, and *confounding*.

Study design

Given the concern that home fortification of iron might increase iron intake to unacceptable levels, we decided to give low-dose-iron MNPs for a period of 8 months. One might wonder whether this period is long enough to show an effect of low-dose-iron MNPs. The Home Fortification Technical Advisory Group (HF-TAG) MNPs guidance recommends a minimum of 60 sachets/6 months and a maximum of 180 sachets/6 months to prevent anaemia[6]. In addition, WHO recommends the use of 90 sachets, in a 6-month period using one MNPs sachet (12.5mg iron) every alternate day, in a population where the prevalence of anaemia is 20% or higher[7]. By giving one sachet every other day for 8 months, we met the minimum requirement for duration given in this guidance.

The intervention study was implemented within the Grain Bank programme, meaning that intervention children received CF in addition to MNPs from the Grain Bank, whereas non-intervention children did not get either MNPs or CF. The observed effect of the MNP intervention can therefore not be fully attributed to MNPs only. In addition, as an embedded intervention study, our level of control on the functionality of the Grain Bank programme (Chapter 4) was limited. The Grain Bank programme staff were responsible for the provision of locally produced CFs, and objective measures of the quality (and duration) of the grain bank intervention and utilization of the CF in our intervention children were not available. As a result, we do not know to what extent the consumption of CF has contributed to the observed effect. In addition, from our observations, compliance with the requirement to distribute local CF varied between different intervention clusters. Roche et al.[3] and Sako et al.[8] also reported challenges in the implementation and sustainability of the Grain Bank programme, related to, among other things, dependence on external resources to subsidize the bartering model due to limited financial and material resources, the food shortage experienced, and reliance on volunteer work by mothers in CF preparation. Therefore, we do not expect that the grain bank programme contributed significantly to the observed effect, and we believe that the home fortification of MNPs is to a large extent responsible for the effect found.

In the effectiveness study, we used a quasi-experimental design where intervention and non-intervention clusters were not randomly assigned. Prior to the onset of the programme, intervention clusters had already been purposively selected by

UNICEF in close consultation with national and local governments[3]. To minimize biases due to potential differences in treatment groups[9, 10], we matched intervention and non-intervention clusters, based on pre-set criteria (Chapter 4) including similar geographical, socio-economic, and ecological conditions, food security status, existence of CBN programmes, and livelihood data. Despite the matching, we could not rule out differences between both clusters in nutritional status and other key characteristics at baseline. However, correcting for baseline performance during analysis helped to reduce the potential differences between the groups[11]. Thus, we controlled for potential differences in the analysis using the difference in differences approach[9]. This is a method that gives a stronger impact estimate than analysis of difference between groups at end line only and helps to elucidate the causal relationships important for public health research[12] and to compare the changes[13] in outcomes over time[9]. In our study, we used the pre-intervention period to monitor differences in morbidity and already observed higher morbidity in intervention children compared to non-intervention. The morbidity observed during the pre-intervention run-in period was used as a proxy for baseline morbidity. To our knowledge, this has not been done in previous studies. We assume that we have made sufficient adjustments to reduce the effects of non-randomization.

Selection bias

Selection bias is a pre-trial bias and occurs when the entry criteria for study participants are inherently different[5]. However, we used similar criteria for selecting all children for both intervention or non-intervention groups, so we do not expect a bias caused by differences in entry criteria in our population. Selection bias can also occur as a result of factors that influence continued participation of persons in a study, for instance, the non-response, the lost-to-follow-up, and the volunteer bias[14]. Our study participants were enrolled on a voluntary basis. Individuals who volunteer for a study might possess different characteristics than those who do not[15]. The household selection procedure was based on the mother's/caregiver's willingness to come to the data collection site (their *kebele*'s health post). Often, households in a *kebele* were widely scattered, and households located far from the health post might have been underrepresented in the study sample. Those households might also neither have been seeking health care nor reached by health education programmes, or might have had less access to food, consequently leading to an underestimation of the nutritional indicators. To overcome this potential selection bias, we carried out a mass awareness campaign, using a minimum of three Health Development Army (HDA) members per *kebele* who were familiar with each household in the *kebele,* distributed brochures (in the local language) about the study to ensure high participation, and invited all mothers of eligible children for screening and enrolment in the study. We assume that this increased parents' awareness[16] and ensured high participation and coverage[17], and we expect the selection bias to be negligible[18, 19].

Refusal to participate in a study may be a potential source of bias. We lost about 279 (11.8% of total) children (Chapter 4) to follow-up during the study for several reasons, including death (30), migration to other areas (31), and refusal (about 218) of mother or caregiver to stay in the study for unknown reasons. Nevertheless, our frequent monitoring and follow-up helped us to minimize the number of children lost to follow-up, thus reducing the possible systematic errors that may occur due to lost-to-follow-up[14]. Studies suggest that frequent monitoring and follow-up encourage participants to stay in the programme[20] and reduce the incidence of lost to follow-up[21]. The use of such methodological approaches increased the strength of our study.

Information bias

Information bias is a classification of error in which bias occurs in the measurement of exposure or outcome[5]. This section discusses the major sources of information bias in our studies, related to reliance on recall data, assessment of adherence and compliance, and measurement of incidence.

For information on age (Chapters 2–4), morbidity (Chapters 2 and 4), dietary intake (Chapters 2 and 3), and MNPs intake (Chapter 5), we relied on the memory of the children's mothers or caretakers. Mothers may have made errors, intentionally (social desirability bias)[22, 23] or unintentionally (recall bias), in their answers, thereby affecting the internal validity of our studies. In rural settings like ours, it is always problematic to figure out the date of birth and the exact age of a child in months. Over- or underestimation of children's nutritional status may happen due to misreporting of age estimates by mothers[24]. In a study using data from Mali, for example, it was found that errors in age estimation led to an underestimation of malnutrition by 10–30%[25]. The intention in our studies was to verify the date of birth by written evidence such as a birth certificate or immunization card, but, for most children, written evidence was not available and we had to rely on the mother's verbal information, assuming that she was able to provide accurate information. Errors in age estimation are often reflected in heaping of birthdays to certain days of the month, heaping of birth months to the month of the survey, and heaping of age in months to whole years[25]. Heaping to certain days of the month is probably less problematic, but heaping in months or years may lead to errors in the estimation of malnutrition prevalence[25, 26]. However, in our data, we observed only a small heaping at 6 months of age (n=488, 24% of the total population) and fewer children at 11 months of age (n=214, 10.5% of the total population). There was no difference between intervention groups, so we expect a negligible impact on our outcomes. The overall prevalence of height-for-age and weight-for-height may, however, be slightly underestimated due to overrepresentation of 6-month-old children, as undernutrition is expected to increase with age[27].

Recall bias might also have occurred in mothers' or caretakers' reporting of children's morbidity. Usually, the recall of morbidity symptoms is strongly affected by the time period of recall, resulting in either overreporting[28]or underreporting. Underreporting is mainly reported as being due to forgetting the event; and the shorter the recall period, the more accurate the information collected will be[29, 30]. The period of recall in children should not exceed 3 days to gather maximum information as suggested by Feikin et al.[29]. We assessed the prevalence and incidence of diarrhoea and flu on the basis of reported conditions and days being ill using a 14-day recall; this may have led to underreporting of child morbidity[30]. We tried to minimize this bias by repeating several similar questions to crosscheck the consistency of responses and used probes/symptom lists to minimize the risk of misreporting[30]. In addition, as the follow-up was repeated every two weeks for 21 rounds, mothers were aware that they had to report illnesses to our field staff and hence we assume that they were able to recall their child's morbidity accurately over the 14 days. Studies report that fever that occurred a few days prior to a survey is much less likely to be recalled than fever that occurred the previous day[29, 31]. Therefore, to reduce recall bias, we used the body temperature measurement on the day of survey to assess fever instead of the reported days that the child had a fever[31]. However, we do not assume a difference in recall bias in morbidity between the intervention and the non-intervention group (Chapter 4)[32].

We measured the incidence ratios using this biweekly data reporting of illness over the previous 14 days. If a child had an episode of an infection at the end of a round (14 days) that continued into a new round, it was calculated as two separate episodes, resulting in double counting. In addition, if a child had two episodes in one round, it was indicated as one episode, resulting in a missed episode. In a study in Pakistan, a diarrhoeal episode was defined as a minimum of 2 days with diarrhoea followed by at least 2 diarrhoea-free days, and an acute respiratory illness episode was defined as a minimum of 2 days with signs followed by a sign-free interval of at least 7 days[33]. We did not follow this structure, and the resulting double counting of episodes and the misreporting of short episodes might have led to an under- or overreporting of incidence ratios[34]. Unfortunately, we do not have any information on the extent to which this double counting or missing of short episodes happened in our study.

Recall bias may also have occurred during the 24hr recall, as we had to depend mainly on the mother's self-reported data. We minimized recall bias due to memory by using multiple pass techniques for the 24hr recall[15] (Chapters 2–3), in which caretakers' memory was supported by asking them to mention step-by-step what food and drinks they had given to the child. The multiple pass technique has been widely used in national surveys and research and is known to reduce recall bias[35-37]. To reduce the chance of missing foods, especially those that are known to be often underreported[35, 36], we included probing questions on foods (meal or snacks) consumed out of home[38]. However, although missing out-of-home consumed food such as fruits[39] and snacks[40] is a well-known error in food consumption studies, in our study population this is assumed to be less of a problem as children below the age of 2 years usually stay at home or around their house unlike, for example, schoolchildren[40]. As we have taken the abovementioned measures to minimize recall bias, we think that our 24hr recalls closely approximate the participants' actual dietary intake (Chapter 3)[41, 42], minimum dietary diversity scores, and IYCF practices (Chapter 2).

Variability of intake is an important issue that needs to be taken into account in food consumption studies, because it affects the validity, reliability, and reproducibility of the results[43-45].

Important variability issues in our studies comprise day-to-day variation and seasonal variation. Chapter 3 is based on data from the Ethiopian NCFS, comprising a 1-day 24hr recall assessed in one season. We were unable to estimate day-to-day variation in our data, but we used the day-to-day variance from data of an intake survey among 6–23-month-old children in Uganda to adjust our intakes and to estimate inadequate and excess intakes[46]. However, our data collected for a large number of survey days (and every day of the week) provided a precise estimate of average intake at the population level[46]; this was advantageous for estimating median serving sizes in Chapter 3. Concerning seasonal variability for the development of FBDRs, the NFCS was conducted in only one season, considered to be the longest lean season in Ethiopia[46]. Other studies show that intake of fruits, vegetables, and grains varies significantly by season[47-49]. Communities that are dependent on rain-fed agriculture experience a shortage period between two harvests when food stocks, mainly grains, are depleted, and such seasons are considered as lean[49]. Food stocks are lower in the lean season compared to the harvest season. Although some vegetables are generally eaten year-round, certain fruits and most vegetables are mainly available in a single season[48], especially in rural areas, making seasonal variation greater. Using only data from this lean season may have resulted in the absence of consumption of foods that would be available in the non-lean season, a reduced number of individuals consuming the foods, particularly fruits, vegetables and grains, and lower amounts consumed compared to the non-lean season. This may have resulted in an underrepresentation of certain foods in our FBDRs and hence a conservative estimation of the potential of FBDRs to achieve nutrient adequacy.

Variability of adherence to treatment may affect the effectiveness of home fortification with MNPs[50]. Assessment of adherence is challenging, especially in complex interventions like ours[51]. Like many other studies, we measured adherence by self-reporting and counting sachets[50, 52-54]. As this assessment depends on the mother's memory and willingness to return empty sachets, adherence may have been underestimated. For instance, there were cases where mothers reported that they had lost the used sachets on the way to the health post when coming for biweekly follow-up. A study in Kenya among children aged 12–23 months also found that self-reporting of adherence or sachet counts may lead to an overestimation of adherence compared to using an electronic device[50]. However, our field staff at *kebele* level provided guidance and close follow-up of the use of MNPs by the mothers, and this, we believe, helped to reduce overestimation. In addition, most studies measure adherence either at the start or the end of the intervention[54, 55], but this approach does not allow fluctuations in adherence and utilizations over time to be detected. We, however, designed a monthly data collection tool, whose use in seven rounds of adherence measurement throughout the intervention period allowed us to capture the changes in adherence and utilization over time[56].

Confounding

Confounding occurs when an observed association is not (only) due to the exposure and the outcome of interest, but (also) to a third factor independently associated with both the outcome of interest and the exposure[5], the so-called mixing of effects. We assumed the following factors to be confounders and describe how we handled those in our study:

- Level of inflammation is considered as a confounder in analysing the effect of an iron intervention[57] and hence needs to be adjusted for when measuring the status of serum ferritin (SF) in the body[58]. The acute phase response – a reaction of the body to inflammation – influences the absorption of iron[57].Ferritin is a positive acute phase protein (APP) that is elevated in the presence of infection[58], masking the presence of iron deficiency. Thus, measurement of one or more APPs in population surveys helps to detect the presence of infection, in the interpretation of iron status[57-59]. C-reactive protein (CRP) and α_1-acid glycoprotein (AGP) are frequently used as APPs in population surveys[57]. CRP rises rapidly at the onset of infection and reaches maximum concentrations between 24 and 48 hours, whereas AGP may take 4–5 days to reach a plateau[58]. In our study, elevated CRP and AGP levels were taken into account using the internal regression correction approach[60] (Chapter 4), for intervention and non-intervention groups as suggested by the BRINDA study[61]. However, we speculate that it is still possible that the corrections might not have removed all the effects of the acute phase response on SF in this population.

- In Chapter 4, we matched the intervention and the non-intervention group at district level, resulting in an equal proportion of children from both regions, but the sub-sample for biochemical assessment was selected by going from study cluster to next nearby cluster, until the required number was obtained. As a result, all the children in the non-intervention group were from SNNP, whereas all but 15 of the children in the intervention group were from Oromia. From our analysis, we observed no improvement in SF in intervention children, whereas the non-intervention children did improve in SF. We assume that this is due to the regional differences between these groups, as reflected in a difference in dietary patterns and staple diets. The nature of the staple diet in SNNP facilitated the bioavailability and absorption of intrinsic iron[62-64]. In addition, the higher prevalence of food insecurity in Oromia during the time of this study is likely to have contributed to the observed difference in iron status among children even at baseline[46].
- In Chapter 2, while investigating the association between potential determinants and nutritional status (stunting and wasting), we took age of child, *kebeles* (clusters), and mother's characteristics into account as potential confounders.

Although we have carefully adjusted for the abovementioned potential confounders, we cannot disregard the possibility of residual confounding due to variables that are not measured or analysed (to date).

External validity

External validity of research deals with what other studies say about the particular topic and the degree to which findings or the inference of causal relationships[65] can be generalized to other groups or populations[5, 66]. It also refers to the *applicability* of interventions in settings beyond the original study[67]. In the next section, first we address the *generalizability* of our study, followed by a discussion of the external validity of our results concerning young child nutrition and the effectiveness of, adherence to, and possible risks of, a low-dose-iron MNP intervention.

Generalizability

We used several entry criteria to admit children into the study, including child's nutritional status. We enrolled apparently healthy children (at least >-3 weight-for-height Z score) and referred children with a ≤-3 weight-for-height Z score to a health facility for treatment, excluding them from the study. Exclusion criteria included the presence of serious disabilities that would affect normal growth and development. This might partly explain why we found stunting and anaemia prevalence lower than the national average[68].

Despite the inclusion of relatively healthy children in the study (Chapters 2 and 3), we do not expect any problems regarding the generalizability of the recommended IYCF practices and FBDRs, respectively, because the children's characteristics are similar to those in other *kebeles* in Ethiopia[46]. Moreover, the selected regions are the largest in the country and represent different local cultures and feeding habits.

Both the intervention and the non-intervention groups (Chapters 4 and 5) were purposively selected from CBN-programme *woredas*, which are selected for such programmes because they are prone to food insecurity[69] and therefore targeted for emergency response and supported by organizations like UNICEF. In addition, as malnutrition rates in these CBN *woredas* are high, infant and young child nutrition (IYCN) programmes are active and on-going in these *woredas*[70], including monthly growth monitoring promotion, targeted counselling (on IYCF and water, sanitation, and hygiene (WASH) practices), community mobilization, and conversations on nutrition (WASH and health issues). Results from our studies should therefore be generalized cautiously to non-CBN *woredas*. Second, in our mixed-methods study (Chapter 5), MNPs were distributed to children free of charge. Consequently, adherence might be higher compared to a situation where mothers would have to pay for the MNPs. Mothers' willingness to pay for MNPs was not considered in this study; however, this willingness could influence the continuity of MNP consumption. The advantages and disadvantages of different MNP delivery models are described elsewhere[71]. Although our study gave an insight into MNP implementation in Ethiopia and factors associated with adherence, using different delivery models will affect adherence to, and effectiveness of, home fortification with MNPs. Finally, our study participants were from rural areas and were mostly illiterate, limiting the extent to which the results are generalizable to urban populations and literate populations.

Young child nutrition

We found a high prevalence of undernutrition in young children (Chapter 2), confirming earlier studies in Ethiopia[72-75]. Area of residence is an important predictor of child nutritional status[76, 77]. In addition, Headey et al.[78] reported children in SNNP, Amhara, and Tigray regions as being more likely to be stunted compared to children from Oromia. We also found that children in SNNP were more stunted than those in Oromia. In addition, we observed that stunting was more prevalent in boys compared to girls. This is consistent with other studies in Sub-Saharan African countries[79, 80], including a study in northwest Ethiopia reporting a lower mean HAZ score in boys compared to girls[74]. Our study showed that poor IYCF practices in the study *kebeles*/clusters were reflected by a low dietary diversity and a low percentage of children receiving a minimum acceptable diet[81]. Our findings are consistent with studies reported from other parts of Ethiopia[82, 83]. Although poor IYCF practices were observed in both boys and girls, predictors of stunting were not completely similar for each gender. Among IYCF practices, early initiation of breastfeeding (IBF) and the status of exclusive breastfeeding (EBF) were significant predictors of stunting in boys but not in girls, whereas timely introduction to CF was a common significant predictor of stunting. Only early IBF tended to be different for boys and girls in analysis of interaction terms for stunting and gender. This may suggest a higher vulnerability to poor feeding practices before 6 months of age among boys compared to girls. IBF, EBF, and timely introduction to CF are important factors in protecting the child against the risk of childhood diseases, including infectious diseases and malnutrition[84]. Several other studies also confirm the importance of EBF for the first six months of life in reducing stunting[85]. The association of stunting with other factors[86-88], including a range of infectious disease[89, 90], also confirms the importance of EBF. The low levels of IBF, EBF, and timely introduction of CF confirm the need for updated guidelines for feeding infants and young children in Ethiopia. We also found regional differences in IYCF, similar to other studies reporting differences in food preferences[91] and differences in food culture[92-94]. Given the observed regional and gender differences in nutrition status and IYCF, the development of contextualized and gender-sensitive guidelines for optimum IYCF, including improving maternal (and paternal) awareness[73] of IYCF practices[78, 95], is required to prevent nutritional deficiencies and their consequences.

Our study shows that FBDRs based on local foods alone would not be able to meet nutrient adequacy for all nutrients for children aged 6–23 months, not even if the FBDRs were fully adopted. Optimized local diets did not provide adequate zinc in all regions and age groups or iron in all regions for infants <12 months of age. In addition, nutrient inadequacy was observed for other nutrients, including calcium, thiamine, folate, and vitamins B_{12}, and B_6, in some regions and age groups. We found that niacin intake levels were insufficient in all regions. However, as our dietary intake calculation did not take into account intake of tryptophan, which can be converted to niacin in the body[96-98], we may have overestimated the niacin inadequacy. Similar findings have been observed in other studies[99-102], showing that achieving the estimated average requirement, especially for zinc and iron, is difficult in young children. However, we did find that achieving adequate iron intake was not a problem in our children >12 months, reflected by high iron intakes at the age of 12–23 months. A high iron intake was also reported in the Ethiopian NFCS[46] and in other pocket/localized studies in Ethiopia[64, 103, 104]. In contrast, a high prevalence of iron deficiency (44.4%) in Ethiopian children (6–59 months) was reported in the national micronutrient survey[105]. The discrepancy between high iron intakes and at the same time high iron deficiency may suggest the presence of non-nutrient-related iron deficiency caused, for example, by contamination, infestation due to the presence of intestinal parasites, or malabsorption of dietary iron due to inhibitors like phytate[63, 106, 107].

Alternative strategies are needed to complement the diet to achieve nutrient adequacy. Our modelling of various nutrition intervention alternatives showed that a combination of regional FBDRs with daily low-iron-dose MNPs for 6–11-month olds and every other day for 12–23-month olds closed the identified nutrient gaps. However, the energy constraints in the modelling exercise limited the use of Sq-LNS for modelling, as this would increase energy intake above the requirements. Nevertheless, Sq-LNS could be an option for emergency nutrition programmes where children do have a low energy intake[108]. Other studies also confirm that interventions, such as MNPs[108, 109] and fortified foods[110], can be used to further improve nutrient adequacy.

Effectiveness, adherence, and possible risks of interventions

The previously mentioned discrepancy of reported high iron intakes in Ethiopian children aged >12 months[46] and the high prevalence of iron deficiency in children aged 6–59 months[105] raise questions around the safety of extra supplementation with iron, for example through home fortification. Our study has shown that MNPs with low dose iron every alternate day has a negligible effect on morbidity. Even though we observed a higher prevalence of diarrhoea in the intervention group compared to the non-intervention group, we did not find a difference in clinic visits between both groups, and the prevalence of diarrhoea became smaller over time, suggesting mildness of the morbidity. A meta-analysis conducted by Salam et al.[111] reported increased diarrhoea after provision of MNPs (containing 12.5mg iron), but this effect was due mainly to an increase in diarrhoea incidence reported in one large study in Pakistan[33]. However, in two smaller studies in Nepal[112] and Bangladesh[113], no increase in morbidity was found.

By providing MNPs in a programme setting with integrated IYCF, we remained close to real-life practice; this was a major strength of our study. Moreover, the study was conducted within a large-scale programme involving a large number of participants (2077 children at end line) and was, to our knowledge, the second largest study after the Pakistan study[33], with good compliance throughout the study period and a response rate of 88.2% at end line. In addition, embedding such research in a large-scale programme has the potential to capture challenges related to operational issues, to promote the sustainability of improvement, and to contribute to policy decisions[22, 65, 114]. It also provides richer information, experience, and insights into effective adaptations of interventions and increases the generalizability of the study[22, 115].

We have demonstrated the effectiveness of an MNP intervention in a programme setting. MNPs with low dose iron, when provided in combination with other IYCF interventions (with the provision of locally processed CF), marginally improved haemoglobin status and resulted in a significant improvement in linear growth (height and weight) in our population. Although a direct association between MNPs and growth is not to be expected[111, 116], it might be possible that the MNP intervention prompted caregivers to feed children more healthy foods. For instance, during the orientation and follow-up, they were informed to use semi-solid foods like porridge made from CF to mix the MNPs, and such orientation might have increased awareness of feeding nutritious foods[117, 118]. Our results are consistent with a limited number of other studies that showed a significant effect of MNPs on growth and reducing anaemia[113, 114, 119], also when provided in combination with other nutrition or hygiene education interventions[109, 113]. A study conducted by Locks et al. also reported the benefit of an integrated (MNPs containing 10 mg iron and IYCF) intervention for 18 months in 6–23-month-old children in Madagascar[118]. The benefits in Madagascar included a reduction in anaemia from 75% to 65% and an increase in nutrition knowledge among mothers. Another health and nutrition programme in rural Haiti, where a 2-month intervention (with MNPs containing 12.5 mg iron and other key micronutrients) was provided to 9–24-month-old children[119], resulted in a reduced (54% to 24%) prevalence of anaemia.

Our study showed a good acceptability of MNPs over time, and most of the mothers perceived positive benefits to the child's health and appearance. However, adherence was found to be low. This might be attributed to the less frequent delivery scheme (bimonthly distribution) and inconsistent instructions on using the MNPs. Low adherence to MNPs was previously reported in Peru, due to misunderstanding on the preparation of MNPs leading to a lower acceptability, and in Aboriginal children due to the mother's forgetfulness[120-122]. Good acceptability of MNPs is consistent with results of earlier studies[54, 55, 122-124]. Compared to our study, the higher frequency of distribution in these studies, monthly and twice weekly, resulted in high consumption (57.6 – of a planned 60 – sachets) in Haiti and a compliance of 100% of MNPs in Lao[119, 125].

Conclusions

This thesis demonstrated high levels of stunting and wasting, especially in boys, associated with feeding practices in the first six months of life. With regard to stunting, poor breastfeeding practices in the first six months of life seemed to have more impact in boys than in girls. Timely introduction of complementary feeding after six months appeared to be a strong predictor of stunting in both boys and girls. We showed that FBDRs could help improve nutrient adequacy during this period, but these FBDRs should be region-specific. We also demonstrated that FBDRs based on local foods alone could not meet the recommended nutrient intake and should be combined with daily (for 6–11 months of age) and every other day (for 12–23 months of age) low-dose-iron MNPs together with breastfeeding on demand during the first two years of life, without risk of excessive iron or zinc intakes. Providing low-dose-iron MNPs every alternate day to 6–11-month-old infants for 8 months in the context of a programme on local production of CFs resulted in improved haemoglobin concentration (not accompanied by iron stores changes) and increased linear growth outcomes, compared to the control group. Although diarrhoea morbidity increased, this increase seemed to disappear over time and may not indicate severe disease. Mothers' acceptability of MNPs was good, although adherence was low mainly because of a less frequent delivery scheme (bimonthly distribution) and inconsistent instructions on using the MNPs.

Public health implications and future research

Based on the findings of this thesis, implications for public health and future areas of research in this field are described below.

Public health implications

- The design of future behaviour change intervention strategies should consider issues related to regional variations and the involvement of social support, for example by involving community leaders in baby care. The observed gender and regional differences also suggest the need for region-specific intervention plans emphasizing gender-sensitive guidance on optimum IYCF practices. A translation of the FBDRs into practical guidelines should also take into account foods that are part of a healthy diet but currently not consumed frequently enough to feature in the models, for example fruits and vegetables. In addition, strategies aimed at improving IYCF practices should be based on formative research on barriers and enablers for mothers to engage in IYCF practices. If food security is an important barrier for mothers, programmes should take this into account and tackle the issue of food security along with behaviour change messages.
- Increasing awareness of communities through behaviour change interventions using different channels as suggested by others is also important for improving compliance with IYCF practices[126-128]. In our study, involving society and improving social support were positive factors associated with adherence. For example, in one of our study clusters, we found eight fathers of the study children who did not allow

mothers to go to the health post to collect MNPs. Through discussions between field study staff and fathers, at least four of them were convinced and allowed the mothers to go to the health post to collect MNPs. A cooking demonstration could also help to clarify doubts about MNP preparation, as suggested by one of the interviewees. Our results suggest that future MNP programmes need to consider factors that positively and negatively affect adherence. For instance, adherence could be improved by 1) empowering fathers and health workers to be more involved in the programme and 2) including the social environment in behaviour change campaigns and adapting dosing regimen and instructions.

- Proper packaging of MNPs, use of the local language, and clear instructions concerning dosage and administration are required for successful MNP implementation. We observed the benefit of intermittent administration rather than daily MNP use. Frequent and flexible administration[129] of MNPs (monthly instead of every 2 months) is further recommended to improve adherence[130, 131].
- We noted that an integrated intervention with MNPs adds value in facilitating growth monitoring and promotion services. MNPs along with CF, therefore, have the potential to serve as a trigger for mothers to attend integrated IYCN programme sessions[8] aiming to improve IYCF knowledge and practices[118] with a view to improving the nutritional status of young children in Ethiopia.
- We have shown that low-iron-dose (6mg) MNPs every other day is safe and acceptable in our population. However, programmes introducing higher dose MNPs in the context of an integrated IYCN intervention should ensure adequate monitoring and management of diarrhoea and morbidity[132]. Furthermore, it is recommended to further analyse the risks and benefits associated with MNPs with a higher level of iron (12.5mg iron) in the Ethiopian context, as recommended by WHO, in a well-designed study to understand potential complications from morbidity and mortality, before launching at large scale in Ethiopia.

Future research areas

- The feasibility of the implementation of FBDRs should be assessed by household trials, such as trials of improved practices, in order to identify barriers and supporting factors for adoption of FBDRs. In addition, the cost of the foods should be included to design cost-effective dietary recommendations. Furthermore, it is recommended to study the effect of cost constraints on food choices[133] and evaluate the economic value of proposed interventions.
- Information on the causes/aetiology of anaemia in settings with sufficient iron intake is scarce. A study on causes of anaemia should include analysis of food samples (quantifying iron absorption inhibitors and facilitators)[132] and biomarkers including serum ferritin along with inflammation markers.
- Comparing adherence to the intervention in the context of monthly vs 2-monthly distribution of MNPs is recommended to identify the optimal distribution scheme in terms of compliance, cost-effectiveness, and so forth. In addition, some of the mothers experienced rejection of the food with MNPs by the children due to changes in the taste of the food. Thus, the reason for changes in the taste of food mixed with MNPs may need further investigation.
- The mechanism for delivering MNPs, including place of delivery, cost-effectiveness (willingness to pay), and cost-benefit analysis of implementation, needs to be studied to assess the feasibility of implementation and to scale up implementation[71]. Future studies should also investigate the best approaches to increase/improve adherence to MNPs, including factors associated with health workers[134-136], such as information on health workers' perception of MNPs, the level of support provided by health workers to mothers, and the feasibility of implementing MNPs in tandem with existing CBN programmes.

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Acknowledgments

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I dedicate this work to my late father, Samuel Hafebo whose inspiration and moral support that aspired me to seek for opportunities and endure my challenges to realize his ambition to his daughter.

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This thesis is co-funded by the NUFFIC, Nutrition International (NI) (Global Affairs Canada), NEEP/PATH, NUTRICIA foundation and Van Dam foundation. Gratefully, I would like to sincerely acknowledge the financial contributions of all my funders.

I also received a lot of help from people at Nutrition and Health Division of WUR. My sincere appreciation goes to all members who directly or indirectly involved in my Ph.D. study. I would like to start this by thanking Prof. Frans Kok for the nice welcoming words and encouragement during my first visit to the Netherlands in October 2013. Even if you retired before my completion, your encouraging words at the start of my studies are highly appreciated. I would like to thank Jasmijn, Karen, Gea, Riekie, Rianne, Jacqueline, João, Pim, Jan and Dione for your technical support which made my stay in Wageningen comfortable. I also thank Fré Pepping (VLAG) for your support and curiosity in my achievement. I thank Ilkay Yalim and Jacqueline at IA&S for helping me with the visa issues. I sincerely appreciate Hans Verhoef for your time and valuable explanation and documents shared about iron and data analysis. I would like to thank all the staffs (professors, researchers, dietitians, and technicians) of Nutrition and Health division including the reception staffs of Helix for your support and friendliness during my stay. That meant a lot to me. Thank you!

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I want to thank also Harold van den Berg and Femke in Utrecht, for your concern, hospitality and entertaining me to see that I have a comfortable stay in the Netherlands.

In EPHI I acknowledge the former Director General Dr. Amha Kebede for providing me a support letter and allowing me to pursue my studies. Thank you for your valuable and continued support in my studies even after you left the Institute.

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What else and what not....emmmm, let me finish by saying....

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Aregash

About the author

Aregash Samuel was born on 13 July 1969 in Addis Ababa, Ethiopia. After completing her secondary and high school education in Merti high school, majoring in science stream in 1985, she enrolled for two years diploma in Home Science and Technology by then in Junior College of Agriculture, Hawassa, which is now upgraded to Hawassa University. She then worked as Home Economics teacher for 3 years in Shambu High school, Wollega, Ethiopia. In 1990 she got a scholarship from the Government of India to study B.Sc (Home Science), then in 1994 continued M.Sc in Food Science and Nutrition as a self-sponsored student in India. Her M.Sc Thesis title was "Food product development using composite flours (bread, bun, and naan (Indian flatbread), with different percentage of combination (refined wheat flour, cowpea, and sorghum flour)". After completing her studies she came back to her home country, in 1996 and worked as an instructor of home science-related subjects in Selam Girls Vocational Training Center and as a part-time instructor of Home Science diploma students at Kotebe College of Teacher Education in Addis Ababa for 2 Years. She worked as curriculum developer in areas related to Home economics in the Institute for Curriculum Development and Research (ICDR) and Ministry of Education for more than 7 years, developing Technical Vocational Education and Training (TVET) standards in Food preparation, Textiles and clothing, etc (in 8 occupations). She also worked as accreditation expert in Higher Education Relevance and Quality Agency (HERQA) for 2 and half years. Because of her deep interest to continue in her profession, Aregash then in 2008 moved to Ethiopian Public Health Institute (EPHI) which was used to be Ethiopian Health and Nutrition Research Institute (EHNRI) and working to date as an associate researcher in Food Science and Nutrition Research Directorate. At

EPHI, Aregash also worked as team leader and director of this directorate. She was involved in many nutrition projects as Principal Investigator (PI), Co-PI and collaborator. In August 2013 she was granted NUFFIC scholarship by the Dutch government to pursue her sandwich Ph.D. program at Wageningen University. She has also secured grants from NI Canada, NUTRICIA in the Netherlands and NEEP from Great Britain to conduct the research work. During her Ph.D. study, apart from the fieldwork in Ethiopia, she also co-supervised 8 M.Sc thesis students of Wageningen University. Aregash also attended several national and international conferences within the education programme of the graduate school of VLAG. She also served in organizing committee for MN forum 2014, representing EPHI.

She is a member of Food and Nutrition Society of Ethiopia (FoNSE). She also served as a vice chairman of the Board of trustees for Meserete Kirstos College and a chairman for Board of Fiker Hulegeb Maekel (Loving Holistic center). She is married to Yekunoamlak Alemu, an assistant professor at Addis Ababa University, and they have 1 daughter and 2 sons, Medhanit, Gedion and Mikiyas.

List of publications

Peer reviewed articles

Aregash S. The State of Human Resource Development in the Ethiopian Leather and Leather Products Technology Institute. *The Ethiopian Journal of Higher Education* 2006 Vol, 3, No. 2, 33-68

Masresha T, **Aregash S**, Tsehai A, Tesfaye H, Desalegn K, and Aweke K. Quality of Community Based Nutrition of Integrated Refresher Training Provided for Health Extension Workers in Amhara Region, Northwest Ethiopia. *Current Research in Nutrition and Food Science* 2013 Vol. 1(2), 157-167 http://dx.doi.org/10.12944/CRNFSJ.1.2.07 ISSN:2347-467X, Online ISSN:2322-0007.

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Eileen K, Masresha T, Tesfaye H, Dilnesaw Z, Adamu B, Girmay A, Desalegn K, Tibebu M, Tsehai A, **Aregash S**, Tarik K, Habtamu F, and Joan Van W. Multisector Nutrition Program Governance and Implementation in Ethiopia: Opportunities and Challenges. *Food and Nutrition Bulletin* 2015, Vol. 36(4) 534-548 DOI: 10.1177/0379572115611768

Abinet T, Masresha T, Tesfaye H, **Aregash S**, Tsehay A, Tibebu M, Biniyam T, Dilnesaw Z, Barbara NT and Aweke K. Sensory Evaluation Acceptability for a Food Supplementary Chickpea-Based Ready-to-Use among Moderately Malnourished Children Aged 6-59 months. *Journal of Agricultural Science and Technology* B 5 (2015) 216-230 doi: 10.17265/2161-6264/2015.03.008

Mengistu G, Moges T, **Samuel A**, and Baye K. Energy and nutrient intake of infants and young children in pastoralist communities of Ethiopia. *Nutrition Journal* 2017 Vol 41, 1-6 http://dx.doi.org/10.1016/j.nut.2017.02.012

Tesfaye Hailu, Masresha Tessema, Biniyam Tesfaye, Aweke Kebede, Adamu Belay, Girmay Ayana, Yosef Beyene, Temesgen Awoke, Desalegn Kuche, Andinet Abera, Tsehai Assefa, Dilnesaw Zerfu,

Tibebu Moges, **Aregash Samuel**, Mekonen Tadesse, Tewodros Getachew, Mesret W/Yohanes, Birhanu Wedajo, Mesfin Gose, Barbara Tembo and Yibeltal Assefa.
Effectiveness of Chickpea-Based Ready-to-Use-Supplementary Foods for Management of Moderate Acute Malnutrition in Ethiopia: A Cluster-Randomized Control Trial. EC Nutrition 11.5 (2017): 201-215.

Keflie TS, **Samuel A**, Christine L, et al. (2018) Dietary Patterns and Risk of Micronutrient Deficiencies: their Implication for Nutritional Intervention in Ethiopia. *J Nutrition Health Food Sci* 6(1):1-16 DOI: 10.15226/jnhfs.2018.001120

Tibebeselassie Seyoum Keflie, **Aregash Samuel**, Ashagrie Zewdu Woldegiorgis, Adane Mihret, Markos Abebe, Hans Konrad Biesalski Vitamin A and zinc deficiencies among tuberculosis patients in Ethiopia. J. Clin Tuberc Other Mycobact Dis 12 (2018) 27–33; https://doi.org/10.1016/j.jctube.2018.05.002

Girmay Ayana, Tibebu Moges, **Aregash Samuel**, Tsehai Asefa, Solomon Eshetu and Aweke Kebede. Dietary zinc intake and its determinants among Ethiopian children 6–35 months of age. BMC Nutrition (2018) 4:30
https://doi.org/10.1186/s40795-018-0237-8

Aregash Samuel, Inge D. Brouwer, Edith J.M Feskens, Abdulaziz Adish, Amha Kebede, Luz Maria De-Regil, Saskia J.M Osendarp Effectiveness of a Program Intervention with Reduced-Iron Multiple Micronutrient Powders on Iron Status, Morbidity and Growth in Young Children in Ethiopia. Nutrients 2018, 10 (10), 1508.
https://doi.org/10.3390/nu10101508

Aregash Samuel, Saskia J.M. Osendarp, Elaine Ferguson, Karin Borgonjen, Brenda M. Alvarado, Lynnette M. Neufeld, Abdulaziz Adish, Amha Kebede, Inge D. Brouwer. "Identifying dietary strategies to improve nutrient adequacy among Ethiopian infants and young children using linear modelling."
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Published abstracts

Aregash Samuel, Girma Mamo, Samson Gebremedhin, Tibebu Moges, Tsehai Assefa and Amha Kebede. Effective Modalities to Improve Pregnant Women's Compliance to Daily Prenatal Iron

Supplementation. European Journal of Nutrition & Food Safety, ISSN: 2347-5641, 5(5):778-779, 2015, Article no. EJNFS.2015.283

Masresha Tessema, **Aregash Samuel Hafebo**, Tesfaye Hailu, Desalegn Kuche, Aweke Kebede and Tsehai Assefa. Implementation of Micronutrient Supplementations in Community-Based Nutrition Program in Ethiopia after Integrated Refresher Training (IRT). *European Journal of Nutrition & Food Safety, ISSN: 2347-5641,Vol.: 5, Issue.: 5 (Special issue)*

Dilnesaw Zerfu, Abinet Tekle, Tibebu Moges, Adamu Belay, Andinet Abera, Girmay Ayana, Masresha Tessema, Desalegn Kuche, Meseret W/Yohannes, Amha Kebede and **Aregash Samuel**. The Proportion of Households with Adequately Iodized Salt in Ethiopia. *European Journal of Nutrition & Food Safety, ISSN: 2347-5641,* 5(5): 1120, 2015, Article no.EJNFS.2015.464

Husein Mohammed, Grace Marquis, Frances Aboud, Karim Bougma, Kimberly B Harding, and **Aregash Samuel**. Effect of Early Market Introduction of Iodized Salt on Pregnancy and Birth Outcomes in a Randomized Clinical Trial in the Amhara Region of Ethiopia. Published Online:1 Apr 2017. The FASEB journal. Abstract Number:786.44

Dawd Gashu, Karim Bougma, Kimberly Harding, **Aregash Samuel**, Abdulaziz Adish, Gulelat Desse, and Grace Marquis. Urinary iodine and goiter in preschool children from the Amhara region, Ethiopia (804.23). Published Online:1 Apr 2014. The FASEB journal. Abstract Number:804.23

Expected publications

Aregash Samuel, Saskia J.M Osendarp, Edith J.M Feskens, Azeb Lelisa, Abdulaziz Adish, Amha Kebede, Inge D. Brouwer *(In preparation).* "Gender differences in nutritional status and its determinants among infants (6-11m) in Ethiopia."

Aregash Samuel, Inge D. Brouwer, Nindya P. Pamungkas, Tosca Terra, Azeb Lelisa, Amha Kebede, Saskia J.M Osendarp (*In preparation*). "Determinants of adherence to Micronutrient Powder use among young children in Ethiopia."

Conference presentations (Poster and Oral)

Poster presentations

- **Hafebo, A**., Osendarp, S., Adish, A., Gibbs, M., Kebede A, Wuehler, S., & Brouwer, I. (2015). Can local Diets Meet the Nutrient Adequacy of Young Children in Ethiopia? Evidence from the National Food Consumption Survey. European Journal of Nutrition & Food Safety, 5(5), 910–911. in Addis Ababa, Ethiopia, June 02-06, 2014, ISSN: 2347-5641

- **Aregash Samuel**, Tosca Terra, Inge D. Brouwer, Joanne Leerlooijer, Abdulaziz Adish, Amha Kebede, Saskia J.M. Osendarp. Knowledge, attitude and practices (KAP) of caregivers using MNPs in a program setting in Ethiopia" in Cancun, Mexico, 24-28 October, 2016.

- **Samuel A**, Alvarado BM, Borgonjen K, Adish A, Kebede A, Wuehler S, Osendarp SJM, Brouwer ID. Promotion of local foods with provision of MNPs or sq-LNS can improve nutrient adequacy for 6-23 month old children in Tigray, Ethiopia " in Cancun, Mexico, 24-28 October, 2016.

- **Aregash Samuel**, Saskia J.M. Osendarp, Edith JM Feskens, Abdulaziz Adish, Aikaterina Zarifopoulou, Amha Kebede, Inge D. Brouwer. Effectiveness of a program intervention with reduced-iron MNPs on morbidity, iron status and child growth in young children in Ethiopia at IUNS 21st International Congress of Nutrition, in Buenos Aires, Argentina, 15-20 October, 2017.

- **Aregash Samuel**, Saskia J.M. Osendarp, Elaine Ferguson, Karin Borgonjen, Brenda M. Alvarado, Lynnette M. Neufeld, Abdulaziz Adish, Amha Kebede and Inge D. Brouwer. Identifying dietary strategies to improve nutrient adequacy among Ethiopian infants and young children using linear modelling at IUNS 21st International Congress of Nutrition, in Buenos Aires, Argentina, 15-20 October, 2017.

- **Aregash Samuel**., Saskia JM Osendarp, Elaine Ferguson., Karin Borgonjen, Brenda M. Alvarado, Lynnette M. Neufeld, Abdulaziz Adish, Amha Kebede, Inge D. Brouwer. "Identifying dietary strategies to improve nutrient adequacy among Ethiopian children using linear modelling" at the conference organized by American Society for Nutrition (ASN) in Boston, USA, 9-12 June, 2018.

Oral presentations

- An oral presentation entitled **"Effectiveness of low dose-MNPs on morbidity, iron status and growth in Ethiopian children"** at Micronutrient Forum meeting, in Cancun, Mexico, 24-28 October, 2016.

- An oral presentation entitled: **"Determinants of adherence to micronutrient powders among children 6-11 months of age in rural Ethiopia"** at International Union of Nutritional Sciences (IUNS) 21st International Congress of Nutrition, in Buenos Aires, Argentina, 15-20 October, 2017.

- An oral presentation entitled: **"Effectiveness of a program intervention with reduced-iron MNPs on iron status, morbidity, and growth in young children in Ethiopia"** at the conference organized by American Society for Nutrition (ASN) in Boston, USA, 9-12 June, 2018.

- An oral presentation entitled: **"Identifying dietary strategies to improve nutrient adequacy among Ethiopian infants and young children using linear modelling"** at ANEC 8, Addis Ababa, Ethiopia, October 1-5, 2018.

Overview of completed training activities

Discipline specific courses	Institute	Year
12th International course on production and use of food comp data (FOOD COMP)	*WUR*	2013
Assessments of infants and young child feeding using ProPAN tool	*UNICEF*	2013
Optifood training	*WUR*	2013-2014
Agriculture Nutrition linkages	*WUR*	2014
Exposure assessment	*WUR*	*2014*

Discipline specific conferences and meetings	Country	Year
Micronutrient Forum	*Addis Ababa, Ethiopia*	2014
Agriculture, Nutrition and Health (ANH) Academy Week	*Addis Ababa, Ethiopia*	2016
Micronutrient Forum	*Cancun, Mexico*	2016
IUNS 21st International Congress of Nutrition	*Buenos Aires, Argentina*	2017
American Society for Nutrition (ASN)	*Boston, USA*	2018
African Nutrition Epidemiology Conference (ANEC)	*Addis Ababa, Ethiopia*	2018

General courses	Institute	Year
PhD week	*VLAG*	2013
Information literacy and Endnote Introduction	*WUR*	2013
Introduction to data analysis (Erasmus Summer Program)	Erasmus University - NIHES	2014
Regression analysis	Erasmus University - NIHES	2014
Logistic Regression	Erasmus University - NIHES	*2016*
Case control studies	Erasmus University - NIHES	*2016*
Casual inference	Erasmus University - NIHES	*2016*
Casual mediation analysis	Erasmus University - NIHES	*2016*
Markers and prediction research	Erasmus University - NIHES	*2016*
Techniques for writing and presenting a scientific paper	VLAG	*2016*
African Nutrition Leadership Programme (ANLP)	*North-West University*	*2017*
Research data management	*WUR*	*2016*
Last stretch of the PhD programme	*WUR*	*2016*
PhD peer consultation	*WUR*	*2016/ 2017*
Longitudinal data analysis	*Jimma University*	*2017*
Scientific Ethics and GCP training	*EPHI with CDC*	*2018*

Optional courses and activities		
Preparation of PhD research proposal	*HNE, Wageningen*	*2013-2014*
Paper clip discussions	*HNE, Wageningen*	2016/2017
Staff seminar in Human Nutrition	*HNE, Wageningen*	2013/2017
Presentation of research findings at different meetings/workshops in Ethiopia	*Addis Ababa, Ethiopia*	2014 -2018

Colophon

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