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Food Based Complementary Feeding Strategies for Breastfed Infants: What's the Evidence that it Matters?

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Abstract

The period of complementary feeding represents a major portion of the 1000 day critical window and thus impacts a period of substantial and dynamic infant development. This review highlights and synthesizes findings of several recent studies conducted to evaluate food based strategies on outcomes related to micronutrient status, growth and neurocognitive development. Particular emphasis is placed on interventions using meat or fortified products to impact iron and zinc intakes, due to the dependence of breastfed infants on complementary food choices to meet requirements for these two critical micronutrients. Regular consumption of modest amounts of meat or fortified cereals provides adequate absorbed zinc to meet estimated physiologic requirements, whereas homeostatic adaptation to lower zinc intake from unfortified cereal/plant staples is inadequate to meet requirements. Iron fortification of cereals may be somewhat more effective than meat to improve iron status, but neither prevents iron deficiency in breastfed infants, even in westernized settings. Improvements in the quality of complementary foods have had very modest effects on linear growth in settings where stunting is prevalent. Maternal education is strongly associated with both linear growth and with child neurodevelopment. The determinants of early growth faltering are more complex and intractable than 'simple' dietary deficiencies of micronutrients. Solutions to growth faltering in young children most likely need to be multi-factorial, and almost certainly will need to start earlier than the complementary feeding period.

Introduction

Improving the quality of complementary feeding has been cited as second only to improved rates of exclusive breastfeeding as a measure to prevent deaths in young children in low resource settings^{1,2}. Indeed, the period of complementary feeding covers at least half of the "1000 days" critical window, the period from conception to a child's second birthday³, to improve children's health and well-being, if one strictly counts the 18 month period after exclusive breastfeeding from birth through 6 months of age. The reality, however, is that the minority of infants are exclusively breastfed for the first 6 months of life^{4,5}, so the period of complementary feeding actually includes a much larger portion of that window, and thus impacts a period of substantial and dynamic infant development. (**Figure 1**)

The term “complementary foods” has been defined in many ways but generally refers to any nutrient and energy containing solid or semi-solid food or liquid consumed by infants in addition to human milk or formula. The term “weaning foods” is also applied to indicate that this is a transition from the full liquid diet of the young infant to a more diverse diet which eventually merges to become the same as the rest of the family's foods. For the purposes of this brief review, the emphasis is on breastfed infants, for whom complementary foods ideally balance or “complement” the nutritional gaps that develop as a result of the dynamic nutritional composition of human milk and of the nutritional needs of the breastfed infant. Although the variety of food choices for older infants and toddlers range widely in industrialized settings compared to lower resource settings, practices in all settings seem to be strongly influenced by traditions, often more so than biological factors.

The relative nutritional importance of the choice of types of foods differs according to the type of infant feeding that has been undertaken, that is, whether an infant has been exclusively (and adequately) breastfed or has received a standard infant formula. The latter provides generous amounts of all essential micronutrients and thus leaves little risk of micronutrient deficiencies, although there are trade-offs for that benefit. Formula fed infants may be at more risk of over-feeding and discussions regarding complementary feeding for this large group have focused more on choices to minimize excessive weight gain. Of course in the real world, many infants do not fall neatly into one category or the other, especially in industrialized countries. In the U.S., many infants receive a combination of human milk and formula; the balance of the intake coming from each source will largely define the risk of micronutrient deficiencies. Nevertheless, the rates of “breastfeeding only” (no formula) have been steadily increasing in the U.S. The annual “Breastfeeding Report Card” from the Centers for Disease Control and Prevention indicates that nearly half (47%) of all infants in the US are breastfed x 6 months, with 16.3% being exclusively breastfed at 6 months, thus aligning with current recommendations to exclusively breastfeed through about 6 months ^{5,6}. Furthermore, a full quarter of infants in the US are still breastfed at 12 months of age. These figures for breastfeeding in the US emphasize the importance of complementary food choices. The risks of micronutrient deficiencies in breastfed infants are not only relevant to low resource settings, where breastfeeding is more likely to be the norm.

Since breastfeeding is recognized as the gold standard for infant feeding, this review will focus on evidence for the impact of complementary feeding on outcomes related to nutritional status, growth and development in breastfed infants. The discussion is not intended to be a comprehensive review of the fairly extensive literature on complementary feeding, especially in international settings, but rather will highlight and synthesize findings of several recent studies conducted by our research group to evaluate food based interventions on selected outcomes (Table).

Nutritional gaps faced by older breastfed infants

The risk of micronutrient deficiencies in breastfed infants and the dependence on complementary foods has been reviewed extensively ^{7,8}. Iron and zinc are two micronutrients particularly recognized as “problem nutrients” for older breastfed infants ⁹. This is due to a combination of factors. Human milk is very low in iron, and even with its

favorable absorption, the amount is too modest to contribute substantially to nutritional requirements. For the first several months of life, the infant relies on the iron “endowment” at birth, including the stores acquired in utero and that which is available from red blood cells after birth. Without fortification, plant based diets are generally low in iron and/or contain compounds that interfere with its absorption. In low resource settings, the high rates of infection and chronic immunostimulation are likely to stimulate the synthesis of hepcidin, a protein that blocks absorption of iron from the intestine, among other effects ¹⁰. The degree to which chronic “immune-stimulation” in low resource settings contributes to iron deficiency is unquantified, but is likely to be a factor contributing to the very high rates of iron deficiency in young children. By approximately six months of age, breastfed infants become reliant on complementary foods to meet their iron requirements, which are relatively high due to the need to expand their red blood cell mass.

In the case of zinc, the underlying basis for risk of deficiency is different from that of iron. Zinc concentrations in human milk are initially very high and will provide a comfortable margin well above the estimated dietary requirement ¹¹. Due to complex interactions of zinc transporters in the mammary gland ¹², the concentration of zinc in human milk falls precipitously, regardless of maternal dietary zinc intake or status ¹³. By approximately 6 months, intakes from human milk will, like iron, provide only a fraction of estimated requirement. The breastfed infant thus becomes dependent on choice of complementary foods to meet requirements for these two essential trace minerals.

The foods that provide naturally good sources of both iron and zinc are meats/flesh foods and organs such as liver. Traditionally, however, in industrialized countries, these have been among the last foods to be introduced to infants. Instead, iron fortified cereals (and infant formulas) have been the recommended “first food” for infants; these are followed by pureed vegetables and fruits, none of which provide significant amounts of either iron or zinc. Recommendations from the World Health Organization for complementary feeding practices emphasize the importance of daily animal source foods to meet micronutrient needs, including especially iron and zinc. If such foods are not consumed, routine use of supplements or fortified foods is recommended ¹⁴. Although the theoretical benefit of meat as a complementary food is sound, the actual data to demonstrate benefit have been very limited.

Evidence for the micronutrient adequacy of different complementary feeding strategies

Controlled trials comparing complementary feeding strategies to meet iron and zinc needs of older infants are limited. We applied stable isotope techniques to examine the adequacy of complementary foods available in the U.S. which were either fortified (infant cereals) or contained intrinsic, highly bioavailable zinc and iron (meats)^{15,16}. The extent to which an older breastfed infant could adapt to chronic low intakes of zinc by increasing absorption efficiency was also of interest, so we also included a whole grain infant cereal that was fortified with iron but not with zinc. (Table)

In terms of zinc intake and absorption, the results of this study supported the premise that, in combination with ad lib breastfeeding, either meat or a zinc-fortified cereal would approximate intake and absorption similar to the Estimated Average Requirement (EAR)

and physiologic requirements, respectively, of the Institute of Medicine ¹⁷. Reflecting the low concentrations in human milk after 6 months of lactation, the contribution of zinc from breast milk was less than 10% of the day's total intake, even though it was well absorbed. The infants receiving the cereal not fortified with zinc fared less well, with a daily intake that averaged approximately half the EAR, including the zinc from human milk. Absorption efficiency did not adequately compensate for the low intake, and in this group none of the infants' daily absorbed zinc reached the estimated physiologic requirement. The unfortified cereal group tended to have the lowest exchangeable zinc pool (EZP) size, consistent with their significantly lower absorbed zinc ¹⁵.

The findings for iron status were more heterogeneous among these 9-10 month old infants. Iron fortified cereals have traditionally been considered an important means to meet the relatively high iron requirements of the older infant. Although the iron in meat is in the heme form, and is thus much more bioavailable than that of the electrolytic iron fortificant in the cereal, the total amount is less than in typical fortified cereals. Evidence to support the adequacy of meats at feasible intakes as a source of iron was also very limited. As expected, the iron intakes for the infants assigned to the fortified cereals were several-fold higher than that of the infants receiving meats. There were no statistically significant differences among the groups in the mean ferritin levels, but more infants in the meat group had a high soluble transferrin receptor, suggesting more suboptimal iron status. Somewhat surprisingly, however, regardless of feeding group, over a third of these healthy, well-nourished infants were mildly anemic and had evidence of iron deficiency. Dietary iron intake was not correlated with iron status; rate of weight gain between 5 and 9 months was negatively associated with serum ferritin level. These findings emphasize that such factors as the accessible endogenous iron at birth, rate of post-natal growth and infant size, in addition to dietary intake and bioavailability all contribute to infants' iron status¹⁶.

In a larger multi-country cluster randomized trial, we compared the efficacy of a year of daily consumption of 1-1.5 ounces of meat vs a multiple micro-nutrient fortified cereal product on nutritional outcomes, including iron and zinc status, in predominantly breastfed infants and toddlers in low resource settings. This trial was conducted in Guatemala, Democratic Republic of Congo, Pakistan, and Zambia, all sites where stunting rates in the second year of life were above 40% ¹⁸. (Table) Similar to the study of U.S. breastfed infants described above, the iron intake of the fortified cereal group was ~ 3.5 times that of the meat group, and the iron status was more favorable in the cereal group. The rate of iron deficiency, however, was modest in both groups at the end of the intervention period at 18 months, with 27% and 16% in the meat and cereal groups, respectively (p=0.001). Although no control group without any intervention was available for comparison, these rates of iron deficiency are lower than generally expected in such settings, suggesting that the iron status of both groups was improved. Zinc content of the cereal was essentially equivalent to that of the meat, and mean plasma zinc concentrations did not differ by group, although the means were quite low compared to the U.S. infants, possibly reflecting subclinical inflammation ¹⁸.

These studies illustrate several points. First, the absorption efficiency (fractional absorption) of zinc from human milk was relatively high but the actual amount of zinc absorbed was still low and did not adequately compensate for the low intake. This confirms the dependence of

the older infant on complementary food sources to get enough zinc. Additionally, the zinc intake of the unfortified cereal group, which followed a pattern very common in both the U.S. and especially in many developing countries (ad lib human milk, fruits and vegetables and unfortified cereal) resulted in daily absorbed zinc well below the estimated requirement. “Up-regulation” of absorption of the zinc with this dietary pattern was insufficient to meet requirements, leaving this group at clear risk of mild zinc deficiency. In low resource settings, the risk for deficiency is even higher due to greater reliance on unfortified cereal/plant staples and high incidence of diarrhea episodes which often result in increased zinc losses and thus result in a relatively higher requirement. Second, the absorption from the fortified cereal was similar to that of the meat, confirming that zinc fortification of a relatively low phytate food offers an efficacious means of meeting zinc requirements of older infants. Third, with respect to iron, although the meat groups had somewhat more evidence of deficiency, substantial numbers of the infants from all groups were iron deficient. The fact that dietary intakes at or above recommended levels did not assure good iron status illustrates the complexity of iron nutrition in older infants and toddlers, and likely provides further insight into the very high prevalence of deficiency in low resource settings.

The metabolic data comparing food based approaches to complementary feeding indicate that daily intakes of a modest amount of meat are feasible to meet recommended intakes of zinc. However, even with the more favorable bioavailability of heme iron, they may not be sufficient to maintain normal iron stores or, especially to achieve repletion in a state of deficiency. It is also clear, however, that iron status is complicated by factors other than dietary intake.

Evidence for impact of improved complementary feeding on growth

Growth faltering is very common and improving the quality of complementary feeding is one of the strategies often cited to improve growth, specifically to reduce stunting (-2 length-for-age Z score, LAZ). The basis for this emphasis is several-fold. The most prevalent pattern of growth faltering is in linear growth, with overall stunting rates estimated to be approximately 1/3 of infants and children under 5 years of age in low resource settings ¹⁹. Additionally, mean LAZ scores at birth are often below the median and continue to steadily decline through the first 24 months of life, tending to plateau thereafter ²⁰. Since exclusive breastfeeding is recommended for the first 6 months of life, and many efforts have focused on improving this health behavior, the remaining postnatal window of opportunity is from 6-24 months, the period of complementary feeding. Wasting rates are generally much lower than stunting rates, and mean weight for length Z scores are near the median, which suggests that energy intake and quantity of food are less problematic compared to the challenge of providing high quality complementary foods.

The recognition that energy intake is not generally growth limiting, the focus of attention has been on intake of micronutrients and quality of complementary foods, less so than quantity, although the importance of adequate energy intake can't be ignored. As noted above, the WHO recommends daily intake of meats and animal source foods for infants and toddlers as routine complementary foods, the rationale for which is supported by the metabolic studies described above. Evidence for efficacy of meats as complementary foods

to impact growth faltering in low resource settings has been limited primarily to observational and epidemiologic data ²¹⁻²³, many supporting an association of better growth and development with regular consumption of meat. One education intervention in Peru specifically encouraged regular consumption of 'special foods', including daily eggs, fish or chicken liver as a complementary food. Results of this cluster randomized trial included a significant reduction in stunting rates ²⁴.

Lacking, however, had been controlled efficacy trials specifically testing the impact of daily meat consumption on linear growth. We have undertaken two cluster randomized trials in diverse settings with high rates of stunting in which 6 month old infants were provided daily meat for one year; their growth rates were compared to infants who received micronutrient fortified cereal ²⁵. (Table) Although in both studies, both meat and fortified cereal groups likely experienced improvements in their micronutrient status from the interventions, no or modest effects on linear growth velocity and stunting were observed^{18,26}.

Notably in these meat intervention studies, as well as in many other trials testing other interventions to improve complementary feeding ²⁷, the impact on linear growth has been quite modest. Even when statistically significant increases have been achieved ²⁶, the effect size or absolute difference in centimeters has been small ²⁸. Furthermore, none of the interventions have stopped the downward trajectory in LAZ from infancy into the second year of life that is common in austere settings ²⁰. Similarly, interventions in older infants and toddlers to specifically improve micronutrient intakes by home fortification with multiple micronutrient powders have not impacted growth ²⁹. It is also possible that, in settings with early and severe stunting, the nutritional deficits may require higher than normal nutrient needs to provide essentially a therapeutic effect. Simply improving the basic quality of complementary feeding through single foods (e.g. meats) or micronutrient fortified foods thus may not provide a potent enough growth 'signal'. Our interpretation of these observations is that the determinants of stunting are considerably more complex than nutritional intake, including of micronutrients, and nutritional status during the post-natal period. Evidence of this is supported by our observations and experience in Guatemala, where stunting is highly prevalent in infants and toddlers and persists into adulthood. Mean LAZ was already -2 by 6 months, and nutritional interventions initiated at 6 months have had no impact on progressive linear growth failure at 12 and 18 months of age ^{18,30}. Maternal height is strongly correlated with infant length and rate of linear growth^{18,31}. Chronic inflammation, e.g. as associated with environmental enteropathy and intestinal inflammation, has also been suggested to adversely impact linear growth in this age group^{32,33}. Finally, in the multi-country meat vs fortified cereal study, the strongest predictor of linear growth was maternal education¹⁸.

Evidence for impact of improved complementary feeding on neurocognitive development

Compared to investigations of growth and nutritional status, fewer interventions have investigated the impact on neurocognitive development of improving the quality of complementary feeding. Undoubtedly, developmental deficits do not occur in isolation and are strongly correlated with stunting and poverty ³⁴. In the trials described briefly above, we have observed modestly but significantly greater scores on behavioral subscales

(unpublished observation), but no meaningful differences in mental or motor development^{18,26}. One recent study employing lipid-based nutrient supplements or a micronutrient fortified corn-soy flour found no difference in developmental scores in 18 month old Malawians after a year- long intervention, but LAZ gain and maternal education were both significant predictors of developmental outcomes³⁵. In a trial in Indian toddlers, improved complementary feeding alone did not effect development, but complementary feeding guidance along with psychosocial stimulation had a significant effect on the toddlers' mental development compared to children in the control group³⁶. These findings all support the critical importance of maternal education, and there is likely a synergistic effect of higher maternal education, enhanced child psychosocial stimulation, and improved nutritional status on child development, with or without a substantial impact on linear growth.

Summary

The period of complementary feeding encompasses more than half of the “1000 days window of opportunity.” Older breastfed infants are clearly at outstanding risk for iron and zinc deficiencies if complementary food choices do not include rich sources of these micronutrients. This is due to the biology of human milk and the dynamic changes in nutritional requirements during later infancy and toddlerhood. While this risk applies to breastfed infants in industrialized countries, it is likely to be even greater in low resource settings where recurrent infections likely contribute to altered nutrient bioavailability, as for iron due to hepcidin stimulation, and to increased losses, as for zinc due to recurrent diarrhea. Improvements in complementary feeding, both with use of fortified foods or by regular consumption of meats, has been associated with improvements in the nutritional status for both iron and zinc. In three intervention studies, we have demonstrated good acceptance of meat by 6 month old infants, and in many settings, flesh foods and/or organ tissue may be more readily available than fortified food products^{23,25,36}. These beneficial effects warrant continued emphasis on the targeting complementary foods to supply these two critical micronutrients. While improved intakes and status have been achieved, the impact of complementary feeding interventions on stunting, however, has been very modest, suggesting that the determinants of growth are more complex and intractable than ‘simple’ dietary deficiencies of these two micronutrients. Solutions to growth faltering in breastfed infants and young children are likely to need to be multi-factorial, and almost certainly will need to start earlier.

References

1. Jones G, Steketee RW, Black RE, Bhutta ZA, Morris SS. How many child deaths can we prevent this year? *Lancet*. Jul 5; 2003 362(9377):65–71. [PubMed: 12853204]
2. Bhutta ZA, Ahmed T, Black RE, et al. What works? Interventions for maternal and child undernutrition and survival. *Lancet*. Feb 2; 2008 371(9610):417–440. [PubMed: 18206226]
3. Martorell R, Zongrone A. Intergenerational influences on child growth and undernutrition. *Paediatr. Perinat. Epidemiol.* Jul; 2012 26(Suppl 1):302–314. [PubMed: 22742617]
4. Bhutta ZA, Chopra M, Axelson H, et al. Countdown to 2015 decade report (2000-10): taking stock of maternal, newborn, and child survival. *Lancet*. Jun 5; 2010 375(9730):2032–2044. [PubMed: 20569843]

5. U. S. Department of Health and Human Services. The Surgeon General's Call to Action to Support Breastfeeding. U.S.Department of Health and Human Services, Office of the Surgeon General; Washington, DC: 2011.
6. Centers for Disease Control. [January 24, 2011] Breastfeeding Report Card - United States, 2011. 2011. <http://www.cdc.gov/breastfeeding/data/reportcard.htm>.
7. Dewey KG, Brown KH. Update on technical issues concerning complementary feeding of young children in developing countries and implications for intervention programs. *Food Nutr Bull.* Mar; 2003 24(1):5–28. [PubMed: 12664525]
8. World Health Organization. Complementary feeding of young children in developing countries: A review of current scientific knowledge. World Health Organization; Geneva: 1998.
9. Gibson RS, Ferguson EL, Lehrfeld J. Complementary foods for infant feeding in developing countries: their nutrient adequacy and improvement. *Eur. J. Clin. Nutr.* Oct; 1998 52(10):764–770. [PubMed: 9805226]
10. Fleming RE, Bacon BR. Orchestration of iron homeostasis. *N. Engl. J. Med.* Apr 28; 2005 352(17):1741–1744. [PubMed: 15858181]
11. Krebs NF, Hambidge KM. Complementary feeding: clinically relevant factors affecting timing and composition. *Am. J. Clin. Nutr.* Feb; 2007 85(2):639S–645S. [PubMed: 17284770]
12. Kelleher SL, Lonnerdal B. Molecular regulation of milk trace mineral homeostasis. *Mol. Aspects Med.* Aug-Oct; 2005 26(4-5):328–339. [PubMed: 16098572]
13. Krebs NF, Reidinger CJ, Hartley S, Robertson AD, Hambidge KM. Zinc supplementation during lactation: effects on maternal status and milk zinc concentrations. *Am. J. Clin. Nutr.* May; 1995 61(5):1030–1036. [PubMed: 7733024]
14. PAHO/WHO. Guiding Principles for Complementary Feeding of the Breastfed Child. PAHO, WHO; Washington, DC: 2003.
15. Krebs NF, Westcott JE, Culbertson DL, Sian L, Miller LV, Hambidge KM. Comparison of complementary feeding strategies to meet zinc requirements of older breastfed infants. *Am. J. Clin. Nutr.* May 30. 2012 96:30–35. [PubMed: 22648720]
16. Krebs NF, Sherlock LG, Westcott J, et al. Effects of different complementary feeding regimens on iron status and enteric microbiota in breastfed infants. *J. Pediatr.* Aug; 2013 163(2):416–423. e414. [PubMed: 23452586]
17. Food and Nutrition Board, Institute of Medicine. Dietary Reference Intakes for Vitamin A, Vitamin K, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc. National Academy Press; Washington, DC: 2001.
18. Krebs NF, Mazariegos M, Chomba E, et al. Randomized controlled trial of meat compared with multimicronutrient-fortified cereal in infants and toddlers with high stunting rates in diverse settings. *The American journal of clinical nutrition.* Oct; 2012 96(4):840–847. [PubMed: 22952176]
19. Black RE, Allen LH, Bhutta ZA, et al. Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet.* Jan 19; 2008 371(9608):243–260. [PubMed: 18207566]
20. Victora CG, de Onis M, Hallal PC, Blossner M, Shrimpton R. Worldwide timing of growth faltering: revisiting implications for interventions. *Pediatrics.* Mar; 2010 125(3):e473–480. [PubMed: 20156903]
21. Marquis GS, Habicht JP, Lanata CF, Black RE, Rasmussen KM. Breast milk or animal-product foods improve linear growth of Peruvian toddlers consuming marginal diets. *Am. J. Clin. Nutr.* Nov; 1997 66(5):1102–1109. [PubMed: 9356526]
22. Morgan J, Taylor A, Fewtrell M. Meat consumption is positively associated with psychomotor outcome in children up to 24 months of age. *J. Pediatr. Gastroenterol. Nutr.* Nov; 2004 39(5):493–498. [PubMed: 15572888]
23. Krebs NF, Mazariegos M, Tshefu A, et al. Meat consumption is associated with less stunting among toddlers in four diverse low-income settings. *Food and Nutrition Bulletin.* Sep; 2011 32(3): 185–191. [PubMed: 22073791]
24. Penny ME, Creed-Kanashiro HM, Robert RC, Narro MR, Caulfield LE, Black RE. Effectiveness of an educational intervention delivered through the health services to improve nutrition in young

- children: a cluster-randomised controlled trial. *Lancet*. May 28; Jun 28; 2005 365(9474):1863–1872. [PubMed: 15924983]
25. Hambidge, Sheng; Mazariegos, et al. Meat as a first complementary food for breastfed infants: Impact on iron intake. *Nutr. Rev.* 2011 Accepted for publication.
 26. Tang M, Sheng X, Krebs NF, Hambidge KM. Meat as complementary food for older breastfed infants & toddlers: a randomized control trial in rural China. *Food Nutr Bull.* In press.
 27. Dewey KG, Adu-Afarwuah S. Systematic review of the efficacy and effectiveness of complementary feeding interventions in developing countries. *Matern Child Nutr.* Apr; 2008 4(Suppl 1):24–85. [PubMed: 18289157]
 28. Imdad A, Yakoob MY, Bhutta ZA. Impact of maternal education about complementary feeding and provision of complementary foods on child growth in developing countries. *BMC Public Health.* 2011; 11(Suppl 3):S25. [PubMed: 21501443]
 29. De-Regil LM, Suchdev PS, Vist GE, Walleser S, Pena-Rosas JP. Home fortification of foods with multiple micronutrient powders for health and nutrition in children under two years of age (Review). *Evid Based Child Health.* Jan; 2013 8(1):112–201. [PubMed: 23878126]
 30. Mazariegos M, Hambidge KM, Westcott JE, et al. Neither a zinc supplement nor phytate-reduced maize nor their combination enhance growth of 6- to 12-month-old Guatemalan infants. *J. Nutr.* May; 2010 140(5):1041–1048. [PubMed: 20335626]
 31. Hambidge KM, Mazariegos M, Kindem M, et al. Infant stunting is associated with short maternal stature. *J. Pediatr. Gastroenterol. Nutr.* Jan; 2012 54(1):117–119. [PubMed: 21866055]
 32. Kosek M, Haque R, Lima A, et al. Fecal markers of intestinal inflammation and permeability associated with the subsequent acquisition of linear growth deficits in infants. *The American journal of tropical medicine and hygiene.* Feb; 2013 88(2):390–396. [PubMed: 23185075]
 33. Liu JR, Sheng XY, Hu YQ, et al. Fecal calprotectin levels are higher in rural than in urban Chinese infants and negatively associated with growth. *BMC Pediatr.* 2012; 12:129. [PubMed: 22917269]
 34. Grantham-McGregor S, Cheung YB, Cueto S, Glewwe P, Richter L, Strupp B. Developmental potential in the first 5 years for children in developing countries. *Lancet.* Jan 6; 2007 369(9555): 60–70. [PubMed: 17208643]
 35. Phuka JC, Gladstone M, Maleta K, et al. Developmental outcomes among 18-month-old Malawians after a year of complementary feeding with lipid-based nutrient supplements or corn-soy flour. *Matern Child Nutr.* Apr; 2012 8(2):239–248. [PubMed: 21342456]
 36. Vazir S, Engle P, Balakrishna N, et al. Cluster-randomized trial on complementary and responsive feeding education to caregivers found improved dietary intake, growth and development among rural Indian toddlers. *Matern Child Nutr.* Jan; 2013 9(1):99–117. [PubMed: 22625182]

1000 Days Critical Window

Figure.

Conceptual diagram for post-natal phases of the 1000 Days Critical Window on iron and zinc status, risk of deficiencies, potential impact of complementary feeding on outcomes. Abbreviations: EBF=exclusively breast fed; Zn=zinc; Fe=iron; CF=complementary foods; LAZ=length-for-age Z score

Table 1

Summary of highlighted complementary feeding interventions

Study	Setting	Subjects	Intervention	Outcomes	Results / Comments
Krebs NF, et al (15, 16)	Denver, CO, USA	42, 5-9 month old breastfed (only) infants	Randomized to first CF of meat (M), iron & zinc fortified infant cereal (IZFC), or iron-fortified cereal (IFC)	Dietary intake Zinc absorption (CF + human milk) Zinc & iron status at 9 months of age	<ul style="list-style-type: none"> • Zinc intake & daily absorbed zinc for M and IZFC group significantly greater than IFC group; • Zinc absorption for IFC only ~ 50% of physiologic requirements • Iron intake IZFC & IFC group significantly greater than M group • M group had more infants with elevated soluble transferrin receptor • Independent of group, ~ 1/3 of subjects were iron deficient, 36% anemic
Krebs NF, et al (18)	Guatemala, Democratic Republic of Congo, Zambia, Pakistan	20 clusters / arm; 1062 infants (n=530 meat, n=532 cereal); 6-18 month olds	Cluster randomized efficacy trial: daily meat vs multiple micronutrient fortified cereal $\times$ 1 yr	<ul style="list-style-type: none"> • Linear growth velocity • Micronutrient status • Neurocognitive development (Bayley Scales of Infant Development) 	<ul style="list-style-type: none"> • No difference by group in linear growth • From baseline (6 months) to 18 months, stunting rates increased from 33% to ~ 50% (not different by group) • Maternal education and maternal height positively associated with linear growth velocity • Anemia rates did not differ by group; iron deficiency was lower in cereal group • Mental and psychomotor scores not different between groups (behavior scale favored meat group)
Tang M, et al (26)	Yunnan Province, China	20 clusters, meat (n=514); 40 clusters cereal (n=957) 6-18 month olds	Cluster randomized trial: daily meat (M) vs cereal (C) $\times$ 1 yr	<ul style="list-style-type: none"> • Linear growth velocity • Neurocognitive development (Bayley Scales of Infant Development) 	<ul style="list-style-type: none"> • Linear growth of M group greater than C group • LAZ negative at 6 months & continued to decline over course of study • Mental and psychomotor scores slightly but significantly favored meat group