

IS THE INCLUSION OF ANIMAL SOURCE FOODS IN
FORTIFIED BLENDED FOOD JUSTIFIED?

by

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Abstract

Fortified blended foods (FBF) are used for the prevention and treatment of moderate acute malnutrition (MAM) in nutritionally vulnerable individuals, particularly children. A recent review of current FBF recommended the addition of animal source food (ASF), in the form of whey protein concentrate (WPC), to FBF, especially corn soy blend. The justifications for this recommendation include the potential of ASF to increase length, weight, muscle mass accretion, and recovery from wasting, as well as improve the product protein quality and provide essential growth factors. Evidence was collected from the following four different types of studies: 1) epidemiological, 2) ASF versus no intervention or a low-calorie control, 3) ASF versus an isocaloric non-ASF, and 4) ASF versus an isocaloric, isonitrogenous non-ASF. Epidemiological studies consistently associated improved growth outcomes with ASF consumption; however, little evidence from isocaloric and isocaloric, isonitrogenous interventions was found to support the inclusion of meat or milk in FBF. Evidence suggests that whey may benefit muscle mass accretion, but not linear growth. Overall, there is little evidence to support the costly addition of WPC to FBFs. Further randomized isocaloric, isonitrogenous ASF interventions with nutritionally vulnerable children are needed.

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Chapter 1 - Introduction

Stunting (length-for-age below -2SD) and wasting (weight-for-length below -2SD) affected 165 million and 52 million children, respectively, in 2013¹. Moderate acute malnutrition (MAM) is characterized by a weight-for-length z-score (WLZ) >-3 and ≤-2 ; severe acute malnutrition (SAM) is indicated by a WLZ ≤-3 . Micronutrient fortified-blended foods (FBF) are broadly used to prevent and treat MAM in nutritionally vulnerable individuals, particularly children². The most common types of FBF include corn-soy blend (CSB) and wheat-soy blend (WSB)³.

The United States Aid for International Development (USAID) commissioned a team to analyze current FBF and provide recommendations for improvement⁴. The resulting Food Aid Quality Review (FAQR) recommendations included the addition of 3g of whey protein concentrate with 80% protein content (WPC80) per 100g dry FBF². Justification provided in the report for the addition of WPC80 includes: promotion of linear growth, accrual of lean tissue, increased protein availability, provision of essential growth factors, significant nutrient value in small quantity, and stable price and shelf life². The merit of this justification has been questioned because 1) at the time of the report, whey alone had not been studied in nutritionally vulnerable children, 2) interventions that reported increased linear growth used ASF protein doses greater than the proposed rate of 3%, and 3) growth factor evidence was lacking⁵. Prior to these recommendations, a well-conducted review had determined that, at that time, there was insufficient evidence to justify the inclusion of whey or skim milk powder in FBF for use by nutritionally vulnerable children³.

Although FBF are usually blanket distributed to nutritionally vulnerable regions and given to all household or community members, FBF has the greatest potential to impact the rapid growth of children (birth through adolescence), particularly those highly susceptible to or suffering from MAM. The focus of this review is to determine whether there is now sufficient evidence that animal source foods (ASF), including milk, whey, or meat, improve growth outcomes in nutritionally vulnerable children enough to warrant the inclusion of WPC80 in FBF. Evidence of the additional growth benefits from ASF must clearly offset the increased expense and logistic hurdles of including ASF in FBF.

Chapter 2 - Does evidence suggest additional growth

benefit from ASF?

Epidemiological studies

Various epidemiological study designs over the past 40 years have found a positive correlation between ASF consumption and the linear growth and weight gain of nutritionally vulnerable children (**Table 1**). This section examines the common findings of these epidemiological findings.

There is evidence to suggest that the growth response from ASF is impacted by both the amount of ASF and complementary foods in a child's diet. In one study, weight gain and linear growth were negatively correlated for toddlers in the lowest quartile of dietary ASF (<61 kcal/d), whereas for toddlers with higher ASF intake (>61 kcal/d) the outcomes were positively correlated⁶. Lower infant and toddler milk intake (1.5 servings/day), compared to higher intake (2 servings/day), was associated with a significantly higher incidence of stunting⁷. An analysis of the macrobiotic diets of nutritionally vulnerable Dutch children (0-8 years-old) found that more than 3 servings per day of dairy, compared to 0-2 servings per week, was associated with significantly greater height, weight and mid-upper arm circumference (MUAC), an indicator of body mass growth⁸. ASF was associated with significantly increased linear growth in Peruvian toddlers when total complementary food intake was low, but not high⁹. Liver, pork products, and total animal protein consumption more than once per week, compared to less frequent consumption, was associated with a significantly higher weight-for-age z-score (WAZ) in

nutritionally vulnerable Chinese infants¹⁰. Milk intake was not a reported outcome in this study, likely because of infrequent consumption in the studied population.

A dual-generational prospective cohort study in Guatemala assessed the long-term effects of ASF in FBF¹¹. Female participants of a childhood intervention that compared a dried skim milk beverage to a low-calorie, non-ASF beverage were followed into adulthood¹². As adults, not only were the women who had received dried skim milk (DSM) significantly taller, but they also gave birth to infants with significantly greater birth length than the non-supplemented group's infants¹¹. After correction for maternal height, however, there was no significant difference in infant length. The positive dual-generational linear growth trend supports consumption of DSM in early childhood and the inclusion of DSM in FBF.

ASF consumption in healthy populations has also been associated with increased growth outcomes. A cross-sectional analysis of healthy Danish children found that height was significantly associated with total protein, animal protein, and milk intake, but not with either meat or vegetable protein intake¹³. A study in Iceland found that healthy toddlers with the highest quartile of animal protein consumption, compared to the lowest quartile, had greater weight, height, and BMI at 12 months old¹⁴. A 20-year prospective cohort study in a healthy Danish population found that pregnant women who consumed high amounts of milk (>150ml/day) produced offspring with significantly greater adult height, compared to offspring from mothers who consumed less milk (<150ml/day)¹⁵. Maternal milk consumption has also been associated with significantly higher birth weight elsewhere¹⁶, but this relationship is outside the scope of this review.

A limitation of the epidemiological evidence is that it does not allow for determination of whether the growth outcomes are due to ASF or total dietary protein. It also does not allow for accurate interpretation of whether a specific type of ASF (meat, milk, or WPC) is better than other types. Together, the epidemiologic evidence suggests that higher consumption of milk (2-3 servings/day), total animal protein, and total dietary protein may contribute to increased linear growth in nutritionally vulnerable and healthy children.

Table 1 Epidemiological Studies

Ref	Location	n	Population	Outcomes
6	Solís Valley, Mexico	67	Enrolled at 18 mo., followed 12 mo.	Wt growth slope correlated to total protein g/d, ASF protein g/d, and ASF g/kg. >64kcal/d of ASF: faster linear and wt growth <64kcal/d of ASF: faster linear, slower wt growth
7	Kingston, Jamaica	191	9-24 mo.	Average dairy servings/d: Stunted—1.5 (0-4.0 range) Non-stunted—2.0 (0.5-4.0 range)
8	The Netherlands	243	0-8 yr. consuming macrobiotic diets	Wt, ht, and MUAC ↑ with >3 servings/wk. of dairy versus 0-2 servings/wk.
9	Peru	107	Enrolled at 12-15 mo., breastfed and weaned, followed 3 mo.	ASF associated with linear growth when total complementary food intake was low, not high.
10	Sichuan, China	389	4-12 mo.	↑ WAZ with liver & blood products >1 serving/wk. versus ≤1 serving/wk.
11	Guatemala	263	1. Female adults from a past childhood Atole ^a + DSM vs. Fresco ^b intervention ¹² . 2. Infants of the female participants	↑ ht of female adults with childhood DSM supplementation versus females without childhood DSM supplementation. ↑ birth length in infants born to female adults with childhood DSM supplementation versus infants born to females without childhood DSM supplementation.

Abbreviations: ASF, animal source food; d, day; DSM, dry skim milk; ht, height; kcal, kilocalorie; mo., months; MUAC, mid-upper-arm circumference; ref, reference; wk., week; wt, weight; yr., years

- a. A high-energy, high-protein, fortified, corn-soy beverage
- b. A low-energy sweetened beverage

Intervention trials

There have been a number of intervention trials that have reported growth outcomes from ASF interventions in nutritionally vulnerable children. Early trials compared milk to no intervention or a low-calorie control group^{12,17-24}. Over time, researchers have shifted toward isocaloric interventions²⁵⁻³⁰, and more recently, toward isocaloric, isonitrogenous interventions^{31,32,33} that minimize variables and maximize evidence of a direct effect of ASF. These categories will be discussed from weakest to strongest intervention category for the best interpretation of the ASF effect on childhood growth outcomes.

ASF versus no intervention or low-calorie control

ASF interventions, compared to no intervention or a low-calorie control group, have been cited as supportive evidence for the inclusion of ASF, particularly milk, in the diets of nutritionally vulnerable children (**Table 2**)^{13,27,34,35}. DSM, the most commonly studied ASF in non-isocaloric trials, has consistently and significantly increased the length and weight of toddlers^{17-19,24} and school-aged children^{20,21} when compared to no other dietary intervention.

Evidence suggests that supplementation may have its greatest impact around 12 months of age. Powdered whole milk supplementation significantly increased linear growth and weight gain between 9-12 months of age, compared to 6-9 or 12-36 months of age¹⁹. Additionally, DSM added to a rice-corn-rye-soy cereal resulted in significantly greater linear growth and weight gain in toddlers who enrolled in the study between the ages of 12-14 months, compared to those enrolled between 9-12 months²⁴.

DSM, when compared to no intervention or a low-calorie control, may increase lean body mass (LBM). Skinfold measurements, are an indication of subcutaneous tissue and body fat, whereas mid-upper arm measurements reflect muscle composition³⁶. Compared to no intervention, 10g and 20g of DSM did not increase tricep or subscapular skinfolds of school-age children²⁰. *Atole*, a corn-soy beverage with DSM, compared to *Fresco*, a low-calorie beverage, significantly increased male and female toddler calf circumference and female MUAC and mid-upper arm muscle area (MAMA), another indicator of LBM¹⁷.

A lower incidence of wasting, stunting, and underweight has been associated with ASF. Supplementation with the same *Atole* (DSM) beverage, compared to lower-calorie *Fresco*, significantly prevented²² and increased recovery from¹² MAM wasting in Guatemalan toddlers. A limitation that should be noted about this research is that the size of the studied population was not described²². Additionally, the stunting and underweight incidence in Vietnamese children was significantly reduced with whole milk supplementation compared to no intervention²¹.

Researchers examined the growth effects from incorporating milk, meat, fish, and eggs into macrobiotic diets²³. Parents were given dietary recommendations to add ASF, particularly milk, into the diets of their stunted children (0-8 years-old). Six years after these recommendations, participants had increased their consumption of meat and milk. There was no significant relationship between ASF consumption and male growth. Milk alone, or in combination with other ASF, was associated with significant improvements in female length-for-age z-score (LAZ), WLZ, and MUAC. Meat, fish, or egg, either alone or in combination, were not associated with increased growth²³.

When compared to no intervention or a low-calorie control group, ASF has consistently increased length, weight, and LBM; it has also decreased the incidence of MAM wasting, stunting, and underweight. These outcomes, however, could be attributed to a number of variables including, but not limited to: ASF, DSM, or increased total caloric or protein intake. These results suggest that higher energy consumption corresponds to an increase in all growth outcomes in nutritionally vulnerable children.

Table 2 ASF vs. No Intervention or Control

Ref	Location	n	Entry Age	Duration	Intervention ^a	Outcome(s)
12	Guatemala	372 homes	6-24 mo.	3 mo.	Villages received different beverages, voluntary consumption recorded I. Atole ^b +DSM: 163 kcal/drink, 11.5g II. Fresco ^c : 59 kcal/drink, 0g	Wasting: High participation/consumption with Atole ($\geq 10\%$ energy RDI) increased recovery rate
17	Guatemala	453	Birth	3 yr.	Villages received different beverages, voluntary consumption recorded I. Atole ^b +DSM: 163 kcal/drink, 11.5g II. Fresco ^c : 59 kcal/drink, 0g	Ht, wt: Atole > Fresco LBM: Atole increased calf circumference and female MUAC and MAMA
18	Colombia	131	Birth	3 yr.	Daily family intervention ^d I. DSM, enriched bread, vegetable oil: 3-5 mo.—670 kcal/d, 30.2 g; 6-11 mo.—428 kcal/d, 22.7g; 12-36 mo.—623kcal/d, 30g II. Control, no intervention	Ht, Wt: milk > control growth rates
19	Colombia	232	Birth	3 yr.	Daily I. Whole powdered milk and vegetable mix: 3-6 mo.—670 kcal/d, 22.7g; 6-12 mo.—428 kcal/d, 22.7g; 12-36 mo.—623 kcal/d, 30g II. Control, no intervention	Ht, wt: milk > control Absolute responsiveness greatest between 3-6 mo. Growth responsiveness greatest between 9-12 mo.
20	Bundi, New Guinea	86	7.7-13 yr.	8 mo.	5d/wk, skim milk powder with water or meal I. Control, no intervention II. 10: 98 kcal/d, 10g III. 20: 201 kcal/d, 20g	Wt: 20g > 10g Ht: no difference between interventions TSF & SSF: control > both interventions
21	Vietnam	444	7-8 yr.	6 mo.	6d/wk., (2) 250ml servings/d I. UHT-whole milk: 77kcal/100g, 3g/100g II. Fortified UHT-whole milk: 75kcal/100g, 3.2g/100g III. Control, no intervention	Ht, wt, % underweight, % stunted: milk groups > control
22	Guatemala	n/a	6-48 mo.	3 or 6 mo.	Villages received different beverages, voluntary consumption recorded. Non-wasted children. II. Atole ^b +DSM: 163 kcal/drink, 11.5g II. Fresco ^c : 59 kcal/drink, 0g	Wasting: 3 and 6 mo. of Atole prevented the onset of wasting. Effects greater in children with lower initial WLZ.
23	The Netherlands	209	7-17 yr. (10.9 mean)	6 yr.	Parents of stunted children w/ macrobiotic diets given dietary recommendations, including increase dairy consumption. No control.	Meat and dairy added to diets. Girls—Ht, Wt, MUAC: dairy > (dairy + egg + meat + fish)

24	Ecuador	110	9-14 mo.	11 mo.	5d/wk., non-randomized I. Mi Papilla ^e + DSM: 275 kcal/d, 10g II. Control, no intervention	Boys—no direct relationship with ASF Ht, wt, % underweight: Mi Papilla > control Effects greater in children with older enrollment age (12-14 mo.).
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Abbreviations: d, day; DSM, dried skim milk; ht, height; kcal, kilocalorie; mo., months; ref., reference; SSF, subscapular skinfold; TSF, tricep skinfold; UHT, ultra-heat-treated; WLZ, weight-for-length z-score; wk., week; wt, weight; yr., years

- c. Information represents the distributed amount of each intervention and does not reflect actual consumption. Calories (kcal/d) and protein (g) are indicated after each intervention.
- d. A high-energy, high-protein, fortified, corn-soy beverage
- e. A low-energy sweetened beverage
- f. In addition to the child supplementation, the mothers received intervention food during the third semester prior to the participants' births.
- g. A rice-corn-rye-soy cereal; group selected from poorer communities; control selected from wealthier communities

ASF versus isocaloric non-ASF

Six trials compared ASF to an isocaloric non-ASF intervention (**Table 3**)²⁵⁻³⁰. Every intervention, unless otherwise specified below, was a FBF. All trials that reported weight outcomes found no significant weight gain benefit from the ASF intervention²⁵⁻²⁹. Due to different growth rates throughout childhood, linear and LBM outcomes will be addressed by the enrollment age of study participants: toddler and school-aged.

Of the four toddler trials (6 months-3 years), three reported no difference in growth outcomes between the ASF and non-ASF interventions^{26,29}. A well-controlled trial found no significant difference between lyophilized beef (non-FBF) and rice-soy cereal interventions for linear growth or recovery from stunting and wasting²⁹. The second study reported no linear growth or LBM difference from interventions with or without fish powder, with different base cereals (a corn-soy-peanut cereal and a traditional low-calorie fermented weaning food), and with or without vitamin and mineral fortification²⁶. Although the interventions were isocaloric, the multiple variables limit interpretation of results. In the third study, a millet-based porridge intervention, when compared to additional minced beef, oil significantly increased MAMA and ultra-heat-treated whole milk (UHT-milk) significantly increased MUAC²⁸. There were no significant LBM differences between the UHT-milk and oil. Additionally, no linear growth difference between UHT-milk and oil, or minced beef and oil, was reported. LAZ and linear growth, however, significantly improved with UHT-milk supplementation when compared to minced beef. It should be noted that meat participants consumed significantly fewer daily and intervention calories compared to the oil intervention group.

The fourth toddler trial reported growth differences between ASF and non-ASF supplementation^{28,30}. This trial found that pork (non-FBF) significantly increased the linear growth rate when compared to two non-ASF interventions, a fortified cereal (details not available) and a non-fortified rice³⁰. To date, however, only an abstract has been released.

Two trials enrolled school-aged children (5.5-15.5 years)^{25,27}. Skim milk powder, compared to margarine or additional taro-sweet potato meals, significantly increased linear growth and subscapular skinfolds²⁵. In the second study, UHT-milk, minced beef, or extra oil was added to a maize-bean dish. There were no significant differences between interventions for linear growth or MUAC outcomes, but minced beef significantly increased MAMA compared to oil^{27,37,38}. It should be noted that there was persistent and severe regional drought with food shortages for the duration of this study that may have inhibited the overall growth of the children.

Evidence from isocaloric interventions suggests that skim milk powder or UHT-milk supplementation, compared to oil or energy, may be beneficial for LBM, however, there is limited evidence that milk increases linear growth. No milk protein dose-response relationship has been identified. There is limited evidence that meat supplementation, compared to isocaloric non-ASF or milk interventions, increases growth outcomes in nutritionally vulnerable children.

Table 3 Isocaloric Trials

Ref	Location	n	Entry Age	Duration	Intervention ^a	Outcome(s)
25	Bundi, New Guinea	88	5.5-15.5 yr.	13 wk.	5 d/wk (270 kcal/d) I. Control, no intervention II. Skim milk powder drink: 27.12g [^] III. Extra margarine in meal IV. 5 meals/d instead of normal 3 (actual consumption not monitored)	Wt: milk and margarine no difference between interventions Ht: milk > margarine SSF: Milk > margarine
26	Ghana	190	6 mo.	6 mo.	500g/wk distributed to mothers to feed $\geq 3x/d$ (310 kcal/d) ^b I. Weanimix ^c : 10.7g II. Weanimix + vitamins + minerals: 10.7g III. Weanimix + fish powder: 20g IV. Koko ^d + fish powder: 17.9g V. No Intervention	Wt, Ht, MAMA: no difference between interventions
27, 37, 38	Embu District, Kenya	910	6-14 yr.	2 yr.	5 d/wk during school year (Cohort I—240 kcal/d; Cohort II—313 kcal/d) I. Githeri ^e + minced beef: 19.2g; 21.7g II. Githeri + UHT whole milk: 12.7g; 15.2g III. Githeri + oil: 7.9g; 8.4g IV. Control	Wt, Ht: no difference between interventions MAMA: meat > energy; no difference between milk and energy MUAC: no difference between interventions
28	Embu District, Kenya	554	11-40 mo.	5 mo.	5 d/wk (270 kcal/d) I. Porridge ^f + UHT whole milk: 5.9g II. Porridge + minced beef: 13.0g III. Porridge + added oil & sugar: 3.4g	Wt: no difference between interventions Ht, MUAC: milk > meat; no difference between milk and energy or meat and energy MAMA: energy > meat; no difference between energy and milk
29	Republic of Congo; Zambia; Guatemala; Pakistan	1062	6 mo.	12 mo.	Daily (70kcal/d 6-11 mo.; 105 kcal/d 12-18 mo.) I. Lyophilized beef: 13g; 19.5g II. Cereal ^g : 3g; 4.6g	Wt, Ht, stunting rate, wasting rate: no difference between interventions
30	China	1465	6 mo.	12 mo.	Daily (148 kcal/d) I. Pork: 12.8g [^] II. FC ^h cereal III. Rice ⁱ	Ht: meat > cereal

Abbreviations: d, day; DSM, dried skim milk; ht, height; kcal, kilocalorie; MAMA, mid-upper-arm muscle area; mo., months; MUAC, mid-upper-arm circumference; ref, reference; SSF, subscapular skinfold; UHT, ultra-heat-treated; wk., week; wt, weight; yr., years

- a. Information represents the distributed amount of each intervention and does not reflect actual consumption. Protein (g) is indicated after each intervention.
 - b. Nutrient information was reported per kg of intervention food. Based on amount distributed per week (500g), daily values were calculated.
 - c. A corn-soy-peanut cereal mix
 - d. A low-energy, low-nutrient fermented traditional weaning food, 276 kcal/day
 - e. A local maize-bean dish
 - f. Millet-based porridge
 - g. Rice-soy cereal
 - h. Fortified-cereal-based supplement
 - i. Non-fortified rice supplement
- ^Calculated from United States Department of Agriculture National Nutrient Database: 75g skim milk powder was calculated to have 27.12g protein.

ASF versus isocaloric, isonitrogenous non-ASF

None of the identified isocaloric, isonitrogenous trials intervened with traditional FBF, therefore a brief explanation of the different interventions follows. FBF replace or supplement local dishes to support health and growth, whereas ready-to-use supplementary foods (RUSF) and fortified spreads are complementary foods designed to treat MAM³⁹. They are used for a shorter duration, are more energy and nutrient dense, and are typically more expensive. Ready-to-use therapeutic foods (RUTF), the most energy and nutrient dense formulation, therapeutically treat SAM and are intended as the main, if not only, source of energy during a shorter treatment period³⁹.

Two trials that compared isonitrogenous ASF and non-ASF interventions included a third intervention with a corn-soy blend (CSB) (**Table 4**)^{32,33}. The first trial compared a soy-peanut fortified spread (18.9g protein), a DSM-peanut fortified spread (18.9g protein), and a non-isonitrogenous, non-ASF CSB (34.4g protein)³². The fortified spreads equally and significantly increased weight and MUAC better than CSB; they also had significantly better MAM recovery rates. There was no significant additional benefit from the DSM.

The second trial compared soy-whey RUSF (15g protein), a near-isonitrogenous soy-RUSF (17g protein), and CSB++ (21g protein)³³. CSB++ is a newer corn-soy blend that contains DSM. The CSB++ contained four times less animal protein than soy-whey RUSF and, although not a limiting factor, its lower energy density and added water during preparation required consumption of more than 8 times the quantity of the RUSFs to provide an equal amount of protein and energy. The only whey supplementation benefit was a significantly greater MUAC increase compared to the soy RUSF and CSB++, which did not differ from each

other. There was no significant difference between any intervention for linear growth rate or wasting recovery rate (percent of group recovered). Both RUSF groups gained significantly more weight than CSB++ participants, recovered from MAM wasting significantly earlier, and developed significantly less SAM.

A third isonitrogenous trial examined the efficacy of two soy-based RUTFs (15g protein) with different concentrations of DSM, 10% and 25%, for the treatment of SAM³¹. The 10% DSM intervention, compared to the 25%, had a significantly lower SAM recovery rate and was significantly less effective for weight gain, linear growth, and MUAC gain. Omission of a non-ASF intervention limits the interpretation of these results.

Iso-caloric, isonitrogenous interventions have provided further insight into the effects of ASF on growth outcomes. DSM or whey, compared to an isonitrogenous, non-ASF intervention, provided no additional weight or linear growth benefit. Whey supplementation, compared to isonitrogenous soy supplementation, may increase MUAC; however, because this is the only trial to study whey supplementation in nutritionally vulnerable populations, additional evidence is necessary to determine its efficacy in FBF.

Table 4 Isocaloric, Isonitrogenous Trials

Ref	Location	n	Entry Age	Duration	Intervention ^a	Outcome(s)
31	Malawi	1874	6-59 mo.	≤ 8 wk.	Severely wasted children (175kcal/ kg·d) I. 25% DSM RUTF ^b : 5.49 II. 10% DSM RUTF: 5.49	Ht, wt, MUAC: 25% > 10% Wasting recovery rate: 25% > 10%
32	Malawi	1302	6-60 mo.	≤ 8 wk.	Moderately wasted children (75 kcal/ kg·d) I. DSM + FS ^c : 1.89 II. Soy + FS: 1.89 III. CSB: 3.44	Ht: no difference between interventions Wt, MUAC: both FS > CSB Wasting recovery rate: both FS > CSB; CSB recovery occurred later
33	Malawi	2712	6-59 mo.	≤12 wk.	Moderately wasted children (75 kcal/ kg·d) I. CSB++ ^d : 2.8 II. Soy RUSF: 2.26 III. Soy-whey RUSF: 2	Ht: no difference between interventions Wt: both RUSFs > CSB++ MUAC: soy-whey > soy & CSB++ Wasting recovery rate: no difference between intervention; CSB++ recovery occurred 2 days later Significantly more CSB++ developed SAM

Abbreviations: CSB, corn-soy blend; d, day; DSM, dried skim milk; FS, fortified spread; ht, height; kcal, kilocalorie; mo., months; MUAC, mid-upper-arm circumference; ref, reference; RUSF, ready-to-use supplementary food; RUTF, ready-to-use therapeutic food; SAM, severe acute malnutrition; wk., week; wt, weight; yr., years

- a. Information represents the distributed amount of each intervention and does not reflect actual consumption. Protein (g/ kg·d) is indicated after each intervention.
- b. Soy-based
- c. Peanut-based fortified spread
- d. A corn-soy blend with dried skim milk

Chapter 3 - Additional justification for including ASF in FBF

The FAQR included two additional justifications for the inclusion of ASF in FBF:

1. Improved protein quality and 2. Provision of essential growth factors².

PDCAAS value

According to the 2011 FAQR, the Protein Digestibility-Corrected Amino Acid Score (PDCAAS) of CSB will increase from 0.85 to 0.88 with the addition of 3% WPC80 by weight². PDCAAS, the currently accepted measurement of protein quality and based upon amino acid content and digestibility, is indicative of the amount of protein and its bioavailability. Foods with a PDCAAS greater than 0.80 are considered good protein sources². The Food and Agriculture Organization of the United Nations (FAO) identified three major limitations of the PDCAAS method: (1) overestimation of amino acid absorption, (2) truncation of the score at 1.00, and (3) overestimation of bioavailability⁴⁰. As indicated in a comprehensive PDCAAS review, legume and cereal antinutritional factors—trypsin inhibitors, tannins, and phytates—may reduce amino acid digestibility by up to 50% and protein quality by up to 100%⁴¹. Moreover, the FAO is moving toward a new method of protein quality determination, the Digestible Indispensable Amino Acid Score (DIAAS), which is expected to better account for the PDCAAS method limitations^{40,41}. No evidence was found or included in the FAQR to indicate that the recommended 3% increase in PDCAAS is meaningful enough to increase growth outcomes. Therefore, the recommendation to include WPC80 in FBF, as justified by a 3% increase in PDCAAS, currently lacks evidence.

Growth factors

It is postulated that childhood growth is increased by certain milk components, including growth factors, lactoferrin, bioactive factors, milk peptides, and lactose^{35,41,42}. The term “growth factors” loosely refers to the grouping of hormones, cytokines, and specific proteins, such as insulin-growth factor-1 (IGF-1), that are involved in cellular growth and repair (Gauthier 2006). The FAQR identified IGF-1 as the “essential” growth factor of interest to increase the potential of FBF to effectively manage wasting and promote linear growth².

It is generally accepted that milk stimulates circulating IGF-1, which may in turn increase linear growth^{3,34,43}. Regular consumption of milk or animal protein, but not meat, has been positively associated with increased serum IGF-1¹³. A recent study also associated dairy protein intake with serum IGF-1 levels in six-year-old girls¹⁴. However, seven-day supplementation of casein, but not whey, increased serum IGF-1 in healthy Danish boys⁴⁴. Without the synergistic effect of all milk components, whey’s individual effect on IGF-1 and subsequent growth remains unsupported^{3,42}.

Exercise science researchers have further studied the differential effects between whey and casein, with a focus on their amino acid profiles. Overall, compared to casein, whey improves muscle performance and is absorbed more rapidly, however, no difference in muscle uptake or satiation has been found⁴⁵.

Chapter 4 - Conclusion

The merit of the recommendation to include WPC80 in FBF was questioned based upon three criticisms⁵:

1) At the time of the report, whey alone had not been studied in nutritionally vulnerable children. Matilsky et al., 2009, had in fact studied whey in nutritionally vulnerable children prior to publication of the FAQR³². This trial was mentioned in the FAQR, but its findings were not used as supportive evidence for the report's recommendations, likely because the intervention food was a fortified spread, as opposed to an FBF. No other trials with whey and nutritionally vulnerable children have been identified.

2) Interventions that reported increased linear growth used ASF protein doses greater than the proposed rate of 3%. To include WPC80 at 3% by weight of CSB would provide 2.4g of animal protein, accounting for 13% of the total recommended 18g of protein⁴. The isocaloric trials included in this review that provided sufficient data for calculation used ASF protein doses that ranged from 46.5-100%²⁶⁻³⁰. The two isocaloric, isonitrogenous studies for which a protein dose could be calculated ranged from 13-60%^{32,33}. The whey RUSF that increased MUAC had an ASF protein dose of 13%³³; thus, further investigation is warranted to determine whether the recommended amount of WPC80 would improve growth outcomes.

3) Growth factor evidence was inadequate at the time of publication. While research exists on growth factors, specific evidence of whey's effect on the growth of nutritionally vulnerable children by means of growth factors remains unsupported^{3,35,42}.

The focus of this paper was to review whether there is sufficient evidence that ASF increases growth outcomes in nutritionally vulnerable children. Evidence from all of the intervention trials is summarized in **Table 5**. Epidemiological studies consistently associated improved growth outcomes with ASF consumption; however, there is little evidence from isocaloric and isocaloric, isonitrogenous intervention studies to support the inclusion of meat or milk in FBF. Whey may benefit muscle mass accretion, but not linear growth. The move toward isocaloric, isonitrogenous studies will provide further insight into the extent of milk's impact on growth. The FAQR authors' response to criticism is most relevant for considering the addition of ASF to FBF: "The critical metric is *not* cost per ton of product...but rather cost per impact or effect"⁴⁶. Overall, we conclude from the ineffectiveness of ASF and whey in isocaloric and isocaloric, isonitrogenous intervention studies that the addition of whey and ASF would not positively influence the cost per impact or effect of FBF.

Table 5 Summary of Interventions—did the ASF have a better outcome than the non-ASF?

Study	ASF	Height	Weight	MUAC	MAMA	TSF	SSF	Wasting Rr
ASF vs. Control/No Intervention								
12	DSM							+
17	DSM	+	+	+f	+f			
18	DSM	+	+					
19	Whole powdered milk	+	+					
20	Skim milk powder	-	+			+	+	
21	UHT-whole milk	+	+					
22	DSM							+ (prevention)
23	Meat and dairy	+f	+f	+f				
24	DSM	+	+					
ASF vs. Isocaloric Non-ASF								
25	Skim milk powder	+	-				+	
26	Fish powder	-	-		-			
27, 37, 38^	Minced beef	-	-	-	+			
27, 37, 38^	UHT-whole milk	-	-	-				
28^	Minced beef	-	-		*			
28^	UHT-whole milk	-	-	-	-			
29	Lyophilized beef	-	-					-
30	Pork	+						
ASF vs. Isocaloric, Isonitrogenous Non-ASF								
32	DSM	-	-	-				-
33	Whey	-	-	+				-

Abbreviations: ASF, animal source food; DSM, dried skim milk; MAMA, mid-upper arm muscle area; MUAC, mid-upper arm circumference area; Rr, recovery rate; SSF, subscapular skinfold; TSF, triceps skinfold; UHT, ultra-heat-treated

+ The ASF had a better growth outcome than the non-ASF

+f The ASF had a better growth outcome than the non-ASF for females

- No difference between the ASF and non-ASF

* The non-ASF had a better outcome than the ASF

^Each ASF intervention is included in the table separately, thus, this study is included twice.

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Appendix A - Abbreviations

ASF—animal source food

CSB—corn-soy blend

CSB++—corn-soy blend with dried skim milk

DIAAS—Digestible Indispensable Amino Acid Score

DSM—dried skim milk

FAQR—food aid quality review

FBF—fortified blended food

LAZ—length-for-age z-score

LBM—lean body mass

MAM—moderate acute malnutrition ($WLZ > -3$ and ≤ -2)

MAMA—mid-upper arm circumference

MUAC—mid-upper arm circumference

PDCAAS—Protein Digestibility-Corrected Amino Acid Score

RUSF—ready-to use supplementary food

RUTF—ready-to use therapeutic food

SAM—severe acute malnutrition ($WLZ \leq -3$)

SD—standard deviation

UHT—ultra-heat-treated

USAID—United States Aid for International Development

WAZ—weight-for-age z-score

WLZ—weight-for-length z-score

WPC—whey protein concentrate

WPC80—whey protein concentrate with 80% protein content