Evaluating Growth and Tolerance of Blenderized Tube Feeding Formulas in Children: A Narrative Review of the Literature

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REVIEW

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ABSTRACT

Evidence assessing the safety, efficacy, and growth of children on home enteral nutrition receiving blenderized tube feeding (BTF) formulas is limited. Commercial BTF formulas are now widely available, as are plant-based versions of these formulas as plant-based diets grow in popularity. This narrative review of the literature presents data from the past 25 years on quality of life, clinical, and anthropometric outcomes in children fed BTFs and differentiates between commercial and homemade BTF formulas when possible. Further, while data on plant-based BTFs is limited, this paper discusses challenges and opportunities for clinicians with patients who choose this regimen. The results suggest that both homemade and commercial BTF formulas can promote growth and are often well-tolerated by pediatric patients, though plant-based BTF regimens require close scrutiny and careful monitoring. A nutrition care team should be involved in the planning and monitoring of all patients receiving enteral nutrition at home, particularly those on homemade BTFs and those who follow a plant-based diet.

Key words: Blenderized tube feeding, enteral formula, plant-based, pediatrics, growth.

ABBREVIATIONS

BTF	Blenderized Tube Feeding Formula
SF	Standard Enteral Formula
HEN	Home Enteral Nutrition
GI	Gastrointestinal
AAP	American Academy of Pediatrics
AND	Academy of Nutrition and Dietetics
ASPEN	American Association of Parenteral and Enteral Nutrition
BMI	Body mass index
BTF	Blenderized tube feeding
CBC	Complete blood count
FBDG	Food based dietary guidelines
G-tube	Gastrostomy tube
GERD	Gastroesophageal reflux disease
GI	Gastrointestinal
GI-PedsQL	PedsQL Gastrointestinal Symptoms Scale
HEN	Home enteral nutrition
IQR	Interquartile range
NASPGHAN	North American Society for Pediatric Gastroenterology, Hepatology and Nutrition
Non-GMO	Non-genetically modified organism
OR	Odds ratio
PedsQL	Pediatric Quality of Life Inventory

PGSQ	Pediatric Gastroenterology Reflux Disease Symptoms and Quality of Life Questionnaire
RCT	Randomized controlled trials
RDN	Registered Dietitian Nutritionist
SCFA	Short chain fatty acids
SF	Standard commercial formula
TCA	Taurocholic acid
TMCA	Tauromuricholic acid
TLCA	Taurolithocholic acid
US	United States

INTRODUCTION

Current nutrition trends include a movement toward whole food and plant-based diets for consumers, patients, and clinicians. Interest in whole food and plant-based nutrition, fueled partly by recent Food Based Dietary Guidelines (FBDGs) and recommendations suggesting a shift toward these dietary patterns [1-5], has extended to patients on home enteral nutrition (HEN) [6-8]. Advocates of plant-based diets also cite concerns over environmental sustainability, animal welfare activism, and religious beliefs [4,9]. Homemade blenderized tube feeding (BTF) formulas are not new; these have been used for decades by healthcare professionals, patients, and caregivers who created their own formulas from specific recipes or blending foods from the family meal [10]. Some patients and caregivers choose to use commercially available BTF formulas alone or to augment a homemade BTF regimen [7] and many use a standard commercial formula (SF) as a base and add blenderized whole foods [11]. A survey of 127 parents and caregivers found 89.6% of pediatric patients were provided homemade BTFs for an average of 71% of their daily nutrition [12]. Another recent survey of 433 parents of children on HEN found almost 50% used homemade BTFs for their children [7]. Parents reported the desire to provide whole foods (20%), the decrease in symptoms of intolerance (20%), and dislike of standard formula (20%) among the top 3 reasons for this choice [7]. Clinicians report patients and caregivers are interested in whole food, organic, non-GMO, allergen-free ingredients, and more locally grown foods [7,12-14].

SF became the preferred form of enteral nutrition in the clinical setting due to their sterile nature which alleviated concerns over microbial contamination, while providing specific amounts of macro and micronutrients that would cover patient needs as sole source of nutrition. In line with current trends, there is increasing interest in commercially available BTFs [15]. Homemade BTFs can be labor intensive, require equipment often not covered in medical plans, can cause more frequently clogged tubes, may provide inconsistent nutrient content, and require additional food storage space [8,14,16]. Parents report a lack of knowledge and time constraints as the main reasons they don't use homemade BTFs [7]. Also, some schools do not allow administration of homemade BTFs due to safety concerns, so parents may opt for a commercial BTF formula at school or daycare [17,18].

The resurgence in the application of BTFs for HEN has resulted in a limited body of evidence assessing safety, efficacy and growth in children. A recent literature review on homemade BTFs and commercial BTFs in adults stated that most of the recent literature has focused on the pediatric population, with promising outcomes [19]. The purpose of this narrative review of the literature is to summarize the research specific to growth, tolerance, and clinical outcomes of BTF formulas in children and adolescents. Studies seldom differentiate between the type of BTF formula and may not disclose when a commercial BTF formula is included in a homemade BTF regimen (i.e. used as a nutrient–rich base) or used in addition to a homemade BTF formula (i.e. some portion of the daily feeding). Thus, both commercial and homemade BTF formulas are included in this review. Unlike plant-based milk alternatives whose nutritional inadequacy was recently discussed in the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) Nutrition Committee's Position Paper [20], commercial BTF formulas are typically formulated to provide sole-source nutrition. However, due to the limited lack of available data

on the use of plant versus animal protein-based tube feeding formulas in children, special considerations for clinicians when a pediatric patient will be following a whole food, plant-based enteral diet are proposed.

Search Strategy

A literature search of studies published within the last 25 years on BTFs and plant-based enteral formulas, excluding preclinical studies, was completed using PubMed and SCOPUS databases (Figure 1). The following search terms were used “blenderized tube feeding formula”; “blenderized, pediatric, enteral”; “children, blended, enteral”; “tube feeding formula, growth, plant protein”; “blenderized formula, growth, plant protein”; “vegetarian, children, growth.” Studies were excluded if they were not in children, published prior to 1995, or published in a language other than English. Reference lists from published meta-analysis, systematic and narrative reviews were searched for additional relevant studies. Due to the lack of data on plant-based, BTF formulas the literature search expanded to include reviews of growth and development in children on plant-based diets who do not require enteral feeding. Due to the small sample size of some of the studies included, differences in study design (retrospective, prospective, parental survey), variability in the studied intervention (home blenderized, commercially available), a meta-analysis of available results was discarded.

Results and Discussion of Relevant Outcomes

Results of this review summarize the evidence available in each of the main outcomes or domains that have been studied with BTF. A summary of findings of studies included in this review is available in Table 1.

Effects on Quality of Life

In a prospective cohort study of 70 pediatric patients, Hron, et al. compared pediatric patients receiving at least 50% of their feeding from BTF formulas (homemade or commercial) to those receiving SFs and reported greater satisfaction for those on BTFs (Likert scale 4.3 ± 1.0 vs 3.3 ± 1.2, P = 0.001, higher scores indicating greater satisfaction) [11]. Patients receiving BTFs had a mean age of 4.8 + 3.6 years with wide-ranging indications for enteral nutrition. Patients reported fewer reflux disease symptoms (0.7 ± 0.8 vs 1.2 ± 1.1, P = .007) and fewer total symptom scores (0.8 ± 0.8 vs 1.2 ± 1.0, P = .02) on the Pediatric Gastroesophageal Reflux Disease Symptom and Quality of Life Questionnaire (PGSQ). They also had improved overall gastrointestinal (GI) function using the Pediatric Quality of Life Inventory (PedsQL) (70.2 ± 16.3 vs 62.3 ± 19.6, P = .03). The PedsQL Gastrointestinal Symptoms Scale (GI-PedsQL) showed significant improvement on the following sub-scores: nausea and vomiting (64.0 ± 22.6 vs 49.0 ± 37.9, P = .02), abdominal pain (65.0 ± 26.8 vs 56.4 ± 33.9, P = .04), abdominal upset (65.0 ± 26.8 vs 56.4 ± 33.9, P = .04), diarrhea (87.9 ± 15.5 vs 73.6 ± 26.3, P = .004), worry about stool (91.5 ± 12.8 vs 81.4 ± 30.0, P = .05), and limitations to food and drink (46.1 ± 29.6 vs 29.0 ± 27.6, P = .006) [11]. Trollip et al. surveyed parents of 12 children on HEN and found half of these parents reported an improvement in social inclusion of their children after initiating BTFs (P value not provided) [21]. The evidence to support improvements in psychosocial outcomes, based on a prospective cohort and parent reported survey, while trending toward positive, is limited and of low quality.

Effect on Feeding Tolerance: Upper GI Symptoms

Though limited in quality, evidence supports improvement in enteral feeding tolerance with BTF formulas compared to SF in pediatric patients (7,11,22-25). Increasing oral intake is a main reason cited by many parents for switching their children to homemade BTFs [7,25]. Gallagher, et al. attempted to transition 20 G-tube fed, medically complex, pediatric patients with a mean age of 3.4+2.2 years from SF to homemade BTF formula over a 4-week period [25]. Genetic syndromes and congenital heart disease were the most common primary diagnosis. Patients were followed for 6 months, during which time one patient transitioned to oral feedings and 17 successfully transitioned to homemade BTF formula. Of those 17 who

transitioned, reductions were seen in vomiting (76% to 53%, P = .015) and the use of acid suppression agents (88% to 76%, P = .007). Results showed improved oral intake, nearing significance, in children switched to a homemade BTF formula. Caregivers were surveyed on their perception of G-tube feeding changes over the course of the study, reported significantly less discomfort at six months (5 vs 2, P = .002) and greater satisfaction with feedings (6 vs 9, P < .001) [25]. In a study of 33 pediatric patients with a primary diagnosis of neurodevelopmental delay and post Nissen fundoplication 52% of those fed an individualized homemade BTF formulas had a 76%-100% reduction in gagging and retching, which the authors stated may have decreased oral aversion leading to an improved oral intake in 57% of subjects (P values not reported) [23]. McClanahan, et al. conducted a feeding trial in which 10 children were transitioned from an SF to a plant-based commercial BTF formula over two weeks to assess the effect on tolerance and changes in the gut microbiota over two months [26]. At both the two-week and two-month time points, there was an improvement in constipation (P < 0.001) as stools shifted from hard to soft and formed. Eight of the 10 patients were followed after the study conclusion for a mean of 14 months (range of 6-23 months) and among the 8 families contacted 6 patients remained on the plant-based commercial BTF formula. The two patients who switched from the plant-based commercial BTF formula cited increased bloating and stooling [26]. Of the subjects with GERD (seven of the eight remaining patients), symptoms improved for 4 patients, worsened for 1 patient and did not change for 2 patients (P value not provided). This resulted in 3 patients who were able to stop their GERD medication. For 3 patients with frequent vomiting (3 out of 8 subjects), two reported improvement in symptoms and did not change for 1 patient (P values not provided). A retrospective study of 23 children with a median age of 22 months (interquartile range [IQR] 17–33 months) evaluated changes in symptoms after patients switched to blenderized diet (homemade or commercial BTF formula or a combination of both) from a SF due to tolerance issues [27]. Ninety-five percent of patients who were experiencing upper GI symptoms had improvements within 3 months of initiating BTFs (P value not provided) and over the 12-month follow-up, a logistic regression analysis showed that the odds of a patient having any upper GI symptom decreased significantly (OR 0.37, P < .003) [27]. Two children transitioned exclusively to oral feedings, and caregivers reported oral intake improved in 53% (P value not provided). A survey of 12 parents of children on HEN in Sydney, Australia found the following outcomes in oral intake and restarting oral feedings after initiation of homemade BTF formulas: 5 reporting improvements, 6 stating no change, and 1 reporting a worsening of symptoms [21]. Parents reported the greatest improvements in upper GI symptoms including nausea, vomiting, and reflux after initiating homemade BTFs (P values not provided). Nausea and vomiting, with median score changes from 4 (often) to 2 (rarely), and reflux, with median score changes from 4 (often) to 2.5 (rarely-sometimes), were the most improved. Aspiration also decreased in 4 of 12 children and only increased in 1 after initiation of homemade BTFs (P values not provided). Novak et al., reported anecdotally in their practice that patients on homemade BTF formulas had improved volume tolerance compared to those on SFs [17]. Improved oral intake or tolerance were the most frequently reported upper GI outcomes and all studies reviewed reported a decrease in upper GI symptoms, but evidence in this area is primarily based on parent or caregiver reports.

Effect on Feeding Tolerance: Lower GI Symptoms

Diarrhea and constipation are common concerns in children on tube feedings. Clinician reports of anecdotal evidence of improvements in constipation and diarrhea when switching to a homemade BTF formula from a SF [17] are supported in most trials, parent and clinician surveys, and a case study [11,21,22,24,26]; however, constipation remains an issue in some studies and one recent retrospective study did find an increase in constipation on BTFs [27]. In a 2017 study, Samela, et al. reported children

median age 3.5 years with intestinal failure transitioned from elemental or semi-elemental formulas to a commercial BTF formula with a 90% success rate (9 of 10 children) over an average of 29.2 months [24]. Nutritional needs were met on the commercial BTF formula and patients experienced improvements in stool form and frequency (P values not provided). Supplemental fiber and daily stool softener use previously provided while patients were on the elemental or semi-elemental formulas was eliminated, though occasional administration was reported. Batsis et al. found mild constipation as indicated by a slight decrease in stool frequency and increase in stool firmness occurred in 21% of pediatric patients (n = 5, no P value provided) of pediatric patients who switched to a commercial and/or homemade BTF formulas from an SF; however, the authors reported it was managed through increased water and/or polyethylene glycol (osmotic laxative) [27]. A separate trial of medically complex patients who were transitioned from a SF to homemade BTF formulas found stool consistency and frequency were unchanged; however, stool softener use increased from 24% to 29% (P = 0.022) [25]. In a follow-up assessment of children receiving a plant-based commercial BTF formula, parents reported the formula was well-tolerated and three of five children with constipation experienced long-term improvements after transition from a SF as stools shifted from hard to soft and formed (Bristol Stool scores 3 and 4) (Kruskal-Wallis, P < 0.001) [26]. No patients experienced an increase in lower GI symptoms. In a survey of parents and caregivers of tube-fed children, 42% reported their child fed a homemade BTF had never experienced gastrointestinal symptoms [7]. Of those who did experience symptoms, the most frequently reported included constipation (18.6%) followed by vomiting (13.6%), gas/bloating (11.4%), diarrhea (5.4%), nausea (3.9%), pain (3.9%), and fever (1.1%) with around 10% of those parents attributing the issues to their child's diagnosis and treatment. In the same study, approximately 97% parents of children on exclusively SF reported some symptom of intolerance [7]. Another survey of parents of 12 children (1-14 years) on HEN found both constipation and diarrhea improved after commencement of homemade BTF formulas (P value not provided) [21]. In an open response question, 5 of the 12 respondents stated their child's bowel movements were more "consistent and soft" and most reported either no change or an improvement in abdominal pain. Most evidence, though limited due to sample size and methodology, supports improvements in constipation and diarrhea with BTF formula usage, though the data is inconsistent and more research is warranted.

Anthropometric and Clinical Outcomes

While parents and caregivers regularly report children experience improved growth on a homemade BTF formulas compared to a SF [7,21], there is no data from randomized controlled trials (RCTs) comparing growth outcomes between the two formulas. In a prospective trial of 33 patients post-Nissen fundoplication, Pentiuk et al. reported patients gained an average of 6.2 g/day (median, 5.0 g/day; range, -8.0 to 28.9 g/day) post-surgery while on a homemade BTF [23]. While four children lost weight, three regained the weight and the fourth dropped from the study citing the inconvenience of preparing the diet [23]. A separate prospective study, found that patients required 50% more calories after transitioning to a homemade BTF to maintain their BMI [25]. However, this was the only pediatric study to report a need for increased formula to meet calorie needs in pediatric patients. This same study also found that the proportion of patients with tricep skinfold thickness above the fifth percentile increased from 76 to 82% of patients (P = .001) who transitioned to BTFs over the course of the study. A recent retrospective study in children with a median age of 22 months who transitioned to BTF formulas (commercial and/or homemade) from SFs and were followed for 12 months observed an improvement in weight z-scores between baseline (median, −1.76 [IQR −2.1 to −0.82]) and most recent visit (−1.62 [−2.2 to −0.26]), though the change was not significant (P < .56). There was a significant (P < .017) improvement in height z-scores between baseline (−2.15 [−2.37 to−1.48]) and their most recent visit (−1.56 [−1.85 to −0.08]) after the transition to

BTF [27]. In a separate retrospective chart review of 10 children with intestinal failure who were weaned to a commercial BTF formula from an elemental or semi-elemental formula, age-appropriate weight gain was maintained at six months and at 1 year following the transition [24]. A survey of families of children using homemade BTF formulas found 9 of 12 respondents reported improved growth on homemade BTF formulas compared to SF (P value not provided) [21]. Another survey of parents and caregivers reported children more frequently met growth goals on homemade BTF formulas (89.5%) compared to those on SF (42.9%) [7]. Of these parents, 23.9% reported their child met growth goals on BTF formula but not SF and only 2.5% reportedly met growth goals on SF but not BTF formula [7]. Data on anthropometric changes in children on BTF formulas, while positive, are limited due to study characteristics. Only Gallagher, et al. [25] assessed tricep skinfold thickness and this was the only study to assess anthropometric data beyond weight and height.

Changes in Microbiota

Research also points to potential benefits for the gut microbiota resulting from the prebiotics and phytonutrients from fruits and vegetables included in homemade BTF formulas [28]. In pre-clinical studies, the effect of a plant-based, commercial BTF formula on gut microbiota was assessed in a murine model of colitis in mice [29]. Mice randomized to the plant-based formula experienced better outcomes and had less inflammation than those on traditional enteral formulas or chow. After a seven-day feeding trial, fecal pellets were analyzed using 16S rRNA gene sequences. Microbial patterns clustered separately in the plant-based formula group with increased commensal anaerobes including Clostridiales, Lachnospiraceae, and Rumino. Concentrations of microbial metabolites in the cecal contents of the mice revealed increased amounts of bile acids lithocholate and taurolithocholate and the plant-derived hydroxycinnamic acid, which can have an anti-inflammatory effect and provide protection in colitis models.

Bacterial diversity and richness significantly increased in 20 pediatric outpatients after transitioning to a homemade BTF formula from a SF [24,25]. Proteobacteria in stool samples significantly decreased at six months post-transition ($P = 0.02$) and Firmicutes showed an increasing trend over time ($P > 0.05$) [25]. A study of 10 children assessed the microbial diversity in children receiving SF followed by changes after transition to a plant-based, commercial BTF formula for two months compared to a control of healthy children and found pre-intervention subjects had decreased levels of commensal bacteria and higher concentrations of pathogens [26]. Post-intervention, subject's microbiota resembled healthy controls and the plant-based, commercial BTF formula was reportedly well tolerated with several subjects reporting an improvement in symptoms. Concentrations of short chain fatty acids (SCFAs) pyruvate, acetate, butyrate, and propionate increased at both two weeks and two months after transition to the plant-based, commercial BTF formula, though only the increase in pyruvate was significant. Bile acids did not increase after the intervention and conjugated primary bile acids taurocholic acid (TCA), tauromuricholic acid (TMCA), and taurolithocholic acid (TLCA) were higher in the pre-intervention period. An assessment on the changes in gut microbiota is limited due to the small sample sizes and very limited number of clinical trials.

Clinician's Perspectives

The Committee on Nutrition of the American Academy of Pediatrics (AAP) states commercial BTF formulas are beneficial for pediatric patients with chronic illness who will be on HEN long-term and who have normal digestive function [30]. They noted, however, these formulas may not be well tolerated in patients with compromised GI function who are malnourished. The AAP warned that some homemade "natural food" formulas may be nutritionally inadequate, expensive, and have a high viscosity that could obstruct pediatric enteral feeding tubes. The Committee recommends the involvement of a

registered dietitian nutritionist (RDN) to ensure nutritional adequacy with homemade BTF formulas.

While caregivers often prefer homemade BTF and report increased satisfaction [25], clinicians themselves seem to have mixed feelings on the use of homemade BTF. Patients sometimes report resistance from clinicians when they decide to use homemade BTF and, therefore, choose to "do it alone" without the help of clinicians [14]. A survey of RDNs in Canada found few felt they had the expertise to design, administer, or teach administration of homemade BTF [31]. Only 28% reported being knowledgeable about homemade BTF and only 24% reportedly felt confident managing patients on homemade BTF. In regard to education, 27% of respondents did not have specific BTF education. Those with education on BTF stated it was primarily from informal sources such as self-directed study and learning from colleagues or patients. In the United Kingdom, a 2016 survey of 77 RDNs found 44% would not recommend homemade BTF formulas and 14% would actually recommend against their use [32]. Eighty-two percent reported they never received training on BTF, while 56% had no previous experience with a patient on a homemade BTF. A 2015 survey of 244 RDNs in the US found that 58% use and recommend BTF in their patients and 79% report positive outcomes [33]. The most commonly cited reason for BTF use was parent request (70%) [33].

Potential Risks

There is limited and sometimes conflicting evidence evaluating outcomes associated with the use of homemade BTF formulas compared with SF. Reported potential drawbacks to homemade BTF formulas include inadequate growth, risk of infection, mechanical issues, and cost [8]. One recent US study using current safety standards compared SF, a homemade BTF formula made using baby food, and a homemade BTF formula made with blended whole food and found bacterial counts within the acceptable range and did not detect S. aureus or coliform/E. coli contamination through four hours after delivery to a patient room [34].

Viscosity of homemade BTF formulas may be higher and more likely to cause clogged tubes compared to commercial BTF formulas or SF [14]. Adjusting the fiber content of homemade BTF formulas [17] and using larger feeding tubes of at least 14 Fr can reduce clogging [8,35]. Water may be used to dilute the feeding to decrease viscosity and for flushing; however, excess water can result in a high volume with limited nutrition due to dilution [14]. Diluted feedings can result in weight loss and undernutrition [14,17]. Parent or caregiver error in feeding preparation can also contribute to inadequate nutrient intake (7,17) and nutrient availability varies depending on the cooking method, length and temperature of storage prior to cooking, season in which food is harvested, and the geographical location of the harvested food [36,37]. The American Association of Parenteral and Enteral Nutrition (ASPEN) recommends a RDN or nutrition support clinician be involved in the development of homemade BTF formulas to ensure nutritional adequacy and notes that patients should have proven tolerance to bolus feeds in order to receive homemade BTFs [35].

Infants and young children are particularly vulnerable to nutritional deficiencies resulting in delayed growth from unsupervised homemade BTF formulas. One recent study found patients receiving homemade BTF may require increased calories to maintain BMI z-scores in pediatric patients [25]. Though authors note the reason is unclear, they included the thermic effect of food and alterations in digestion and absorptions due to changes in the diet as possible explanations. In the study, daily energy intake increased 1.5-fold in patients on homemade BTF formulas in order to maintain BMI z-scores. However, body fatness also increased with the use of homemade BTF formula, which suggests that fewer calories might have sufficed.

Safe handling practices of food are required in the preparation, storage, and administration of homemade BTF formulas [35] and clinicians should do more to make parents aware of these risks. If a patient or caregiver decides to initiate or continue to use homemade BTF, the

primary care clinician should consult with an RDN or nutrition support clinician with expertise in homemade BTF [8].

Plant-based Diets and the Pediatric Population

Plant-based SF and BTF are increasingly available in the United States (US). Well-balanced vegetarian diets can meet nutritional needs, but vegan diets are more nutritionally challenging in infants and children [38-40]. Cohen et al., recently presented an abstract of a pea protein-based SF, demonstrating weight gain and improved tolerance in pediatric patients [41]. Soy-based SFs have long been used in enteral nutrition [42,43], but there is a lack of research on whole food- and plant-based enteral formulas in children. While parents who prepare homemade BTFs may opt for vegetarian formulations which include some animal-based proteins such as milk or eggs (lacto-ovo vegetarian), not all commercial BTF formulas currently marketed as “plant-based” are certified as vegan.

Both the Academy of Nutrition and Dietetics (AND) and the AAP state vegetarian diets can meet the needs of children, though they recommend these children should be followed by a RDN [44,45]. Infants and children can achieve plasma biochemical parameters within reference ranges and even preferable blood lipid profiles on non-soy, plant-based formulas or vegetarian diets [46-48], though there are nutritional concerns including reduced intake and absorption of key nutrients [49,50]. Nutrients of particular concern include calcium [48,51-53], vitamin D [51-53], vitamin B12 [53], iron [54], zinc [54,55], and omega-3 fatty acids [56]. Vitamin B12 deficiency is prevalent in infancy for those on a vegetarian diet [49]. Zinc is also potentially problematic as it is required for growth and children do not appear to adapt as easily to a vegetarian diet as do adults through increased absorption of dietary zinc [55]. Heme iron, the most readily absorbed form of iron, is found in meat, poultry, and fish and, thus, not consumed by vegetarians making adequate intake of absorbable iron more difficult. As a result of diets high in iron absorption inhibitors and low bioavailability of non-heme iron, vegetarians iron requirements are 1.8 times higher than omnivores [57].

Growth and development of vegetarian and omnivorous infants and children is generally similar, though height and body weight in vegetarians may be in the lower end of reference ranges [53]. A number of studies found height z-scores within the normal range or comparable between vegetarian and omnivorous children [40,48,53,58-61], but some have found shorter stature in vegan [62] or vegetarian children and adolescents [63,64]. Some studies point to decreased body weight, fat mass and a fat/lean mass ratio in vegetarian children [47,63,65]. However, a systematic review of the literature on children on vegetarian diets noted that these results may be due to selection bias [53]. Messina and Mangels stated that the limited number of well-designed studies assessing growth of children on vegan diets, along with the absence of longitudinal studies, prevent conclusions about growth of vegan children in developed countries [59]. In a more recent review of vegetarian diets in children, Shurmann, Kerting, and Alexy also reported a lack of data allowing for firm conclusions on the effects of the vegetarian diet on children and adolescents in industrialized countries [53].

The AND, in the Evidence Analysis Library, recommends that if dietary intake appears insufficient in the adolescent or child on a vegetarian diet, based on dietary assessment, then biochemical data, medical tests and procedures including, but not limited to, complete blood count (CBC), serum iron, ferritin, transferrin, vitamin B12, zinc, vitamin D and essential fatty acids should be assessed (Rating: Consensus; Imperative) [44]. The recommendation states these nutrients may be of special concern for vegetarians or vegans. AAP’s Committee on Nutrition notes plant-based diets have health benefits, support growth, and can meet the nutritional needs of children, if they are appropriately planned and monitored by a RDN or healthcare professional [45]. The Committee reported children on vegan diets may have slightly higher protein needs due to differences in bioavailability and protein quality and intake of calcium, zinc, and iron should

be emphasized. While these recommendations refer to oral nutrition intake, there is a lack of evidence to support a need for an even higher protein intake in patients receiving nutrition via a feeding tube who are on a vegetarian or vegan diet that is closely monitored by a dietitian, aside from specific conditions. Future studies are needed to assess protein needs with plant-based BTFs.

CONCLUSIONS

Homemade and commercial BTF formulas can support growth and promote tolerance in the pediatric population. While there is limited research on plant-based BTF formulas, a well-designed and monitored, plant- and whole food-based diet for HEN could promote growth and development, though nutrient supplementation or fortification may be required. Commercial BTF formulas are designed as a sole source of nutrition, though some patients may need nutrient supplementation depending on the volume received. Patients on homemade, plant-based BTFs should be monitored closely and will often require nutrient supplementation. HEN should always be monitored by an RDN and this is especially important for patients receiving homemade BTFs or adhering to plant-based diets, as there are special nutritional concerns for each.

Commercial BTF formulas offer a whole food-based, nutritionally consistent and well-defined formula that is microbiologically tested and safe for enteral nutrition. They can be successfully integrated into a feeding regimen with homemade BTFs for the sake of convenience, as required by schools or other caregiver arrangements, or provided on their own to meet nutritional needs. Some patients experience clinical benefits from a partially whole food-based blended diet [14,24], though there is limited data on quantity, frequency, or type of BTF formula needed for optimal clinical outcomes. RCTs comparing outcomes of particular types of BTF formulas and SFs for children are needed. The main limitation of this paper is the lack of RCTs available to complete a systematic literature review or meta-analysis that would strengthen the findings. There is also a lack of studies comparing plant- versus cow's milk protein-based tube feeding formulas to draw conclusions on clinical outcomes, thus extrapolations on the risks and benefits of studies assessing vegetarian diets in children were included. Further studies in this area are warranted. A pragmatic approach to research on BTFs and plant-based diets in children utilizing mixed methods would provide important information on clinical outcomes and the parent or caregiver and child experience with these formulations. Healthcare professionals should educate themselves on the potential risks and benefits of both homemade and commercial BTF formulas, and plant-based diets in their pediatric tube-fed patients.

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REFERENCES

1. Rose D, Heller MC, Roberto CA. Position of the Society for Nutrition Education and Behavior: The Importance of Including Environmental Sustainability in Dietary Guidance. J Nutr Edu Behav. 2019;51(1):3-15.e1.
2. Willett W, Rockstrom J, Loken B, Springmann M, Lang T, Vermeulen S, et al. Food in the Anthropocene: The EAT-Lancet Commission on healthy diets from sustainable food systems. Lancet. 2019;393(10170):447-92.
3. Bechthold A, Boeing H, Tetens I, Schwingshackl L, Nothlings U. Perspective: Food-Based Dietary Guidelines in Europe-Scientific concepts, current status, and perspectives. Adv Nutr. 2018;9(5):544-60.
4. Magkos F, Tetens I, Bugel SG, Felby C, Schacht SR, Hill JO, et al. A perspective on the transition to plant-based diets: A diet change may attenuate climate change, but can it also attenuate obesity and chronic disease risk? Adv Nutr. 2020;11(1):1.9.
5. Wahlqvist ML. Food structure is critical for optimal health. Food Funct. 2016;7(3):1245-50.
6. Hurt RT, Edakkanambeth Varayil J, Epp LM, Pattinson AK, Lammert LM, Lintz JE, et al. Blenderized tube feeding use

in adult home enteral nutrition patients. Nutr Clin Pract. 2015;30(6):824-9.

7. Johnson TW, Spurlock AL, Epp L, Hurt RT, Mundi MS. Reemergence of blended tube feeding and parent's reported experiences in their tube fed children. J Altern Complement Med. 2018;24(4):369-73.
8. Oparaji JA, Sferra T, Sankararaman S. Basics of blenderized tube feeds: a primer for pediatric primary care clinicians. Gastroenterol Res. 2019;12(3):111-4.
9. Sabaté J, Soret S. Sustainability of plant-based diets: back to the future. Am J Clin Nutr. 2014;100(suppl_1):476S-82S.
10. Harkness L. The history of enteral nutrition therapy: from raw eggs and nasal tubes to purified amino acids and early postoperative jejunal delivery. J Am Diet Assoc. 2002;102(3):399-404.
11. Hron B, Fishman E, Lurie M, Clarke T, Chin Z, Hester L, et al. Health outcomes and quality of life indices of children receiving blenderized feeds via enteral tube. J Pediatr. 2019;211:139-45.e1.
12. Epp L, Lammert L, Vallumsetla N, Hurt RT, Mundi MS. Use of blenderized tube feeding in adult and pediatric home enteral nutrition patients. Nutr Clin Pract. 2017;32(2):201-5.
13. Epp L. Blenderized feeding options-the sky's the limit. Pract Gastroenterol. 2018;42(6):30-9.
14. Carter H, Johnson K, Johnson TW, Spurlock A. Blended tube feeding prevalence, efficacy, and safety: What does the literature say? J Am Assoc Nurse Pract. 2018;30(3):150-7.
15. Coad J, Toft A, Lapwood S, Manning J, Hunter M, Jenkins H, et al. Blended foods for tube-fed children: a safe and realistic option? A rapid review of the evidence. Arch Dis Child. 2017;102(3):274-8.
16. Hurt RT, Epp LM, Duellman WM, Pattinson AK, Lammert L, Baker MR, et al. Blenderized tube feedings for adult patients on home enteral nutrition: a pilot study. J Altern Complement Med. 2019;25(4):413-6.
17. Novak P, Wilson KE, Ausderau K, Cullinane D. The use of blenderized tube feedings. ICAN: Infant, Child, & Adolescent Nutrition. 2009;1(1):21-3.
18. Bobo E. Reemergence of blenderized tube feedings: exploring the evidence. Nutr Clin Pract. 2016;31(6):730-5.
19. Brown T, Zelig R, Radler DR. Clinical Outcomes Associated With Commercial and Homemade Blenderized Tube Feedings: A Literature Review. Nutr Clin Pract. 2020;35(3):442-53.
20. Merritt RJ, Fleet SE, Fifi A, Jump C, Schwartz S, Sentongo T, et al. North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition Position Paper: Plant-based Milks. J Ped Gastroenterol Nutr. 2020;71(2):276-81.
21. Trollip A, Lindeback R, Banerjee K. Parental Perspectives on Blenderized Tube Feeds for Children Requiring Supplemental Nutrition. Nutr Clin Pract. 2019;35(9).
22. Johnson TW, Spurlock A, Galloway P. Blenderized formula by gastrostomy tube: A case presentation and review of the literature. Topics in Clin Nutr. 2013;28(1):84-92.
23. Pentiuk S, O'Flaherty T, Santoro K, Willging P, Kaul A. Pureed by gastrostomy tube diet improves gagging and retching in children with fundoplication. J Parenter Enteral Nutr. 2011;35(3):375-9.
24. Samela K, Mokha J, Emerick K, Davidovics ZH. Transition to a tube feeding formula with real food ingredients in pediatric patients with intestinal failure. Nutr Clin Pract. 2017;32(2):277-81.
25. Gallagher K, Flint A, Mouzaki M, Carpenter A, Haliburton B, Bannister L, et al. Blenderized enteral nutrition diet study: feasibility, clinical, and microbiome outcomes of providing blenderized feeds through a gastric tube in a medically complex pediatric population. J Parenter Enteral Nutr. 2018;42(6):1046-60.
26. McClanahan D, Yeh A, Firek B, Zettle S, Rogers M, Cheek R, et al. Pilot Study of the Effect of Plant-Based Enteral Nutrition on the Gut Microbiota in Chronically Ill Tube-Fed Children. J Parenter Enteral Nutr. 2019;43(7):899-911.
27. Batsis ID, Davis L, Prichett L, Wu L, Shores D, Au Yeung K, et al. Efficacy and tolerance of blended diets in children receiving gastrostomy feeds. Nutr Clin Pract. 2020;35(2):282-8.
28. Martin K, Gardner G. Home enteral nutrition: updates, trends, and challenges. Nutr Clin Pract. 2017;32(6):712-21.
29. Yeh A, Conners EM, Ramos-Jimenez RG, Firek B, Novak EA, Rogers MB, et al. Plant-based enteral nutrition modifies the gut microbiota and improves outcomes in murine

models of colitis. Cell Mol Gastroenterol Hepatol. 2019;7(4):872-4.e6.

30. American Academy of Pediatrics Committee on Nutrition. Enteral feeding for nutrition support. In: Kleinmen RD, Greer FR, eds. Pediatric Nutrition. Itasca, IL:American Academy of Pediatrics; 2019.
31. Kariya C, Bell K, Bellamy C, Lau J, Yee K. Blenderized Tube Feeding: A survey of dietitians' perspectives, education, and perceived competence. Can J Diet Pract Res. 2019:80(4)1-5.
32. Armstrong J, Buchanan E, Duncan H, Ross K, Gerasimidis K. Dietitians' perceptions and experience of blenderised feeds for paediatric tube-feeding. Arch Dis Childh. 2017;102(2):152-6.
33. Johnson TW, Spurlock A, Pierce L. Survey study assessing attitudes and experiences of pediatric registered dietitians regarding blended food by gastrostomy tube feeding. Nutr Clin Pract. 2015;30(3):402-5.
34. Johnson TW, Milton DL, Johnson K, Carter H, Hurt RT, Mundi MS, et al. Comparison of microbial growth between commercial formula and blenderized food for tube feeding. Nutr Clin Pract. 2019;34(2):257-63.
35. Boullata JI, Carrera AL, Harvey L, Escuro AA, Hudson L, Mays A, et al. ASPEN safe practices for enteral nutrition therapy. J Parenter Enteral Nutr. 2017;41(1):15-103.
36. Mokhalalati JK, Druyan ME, Shott SB, Comer GM. Microbial, nutritional and physical quality of commercial and hospital prepared tube feedings in Saudi Arabia. Saudi Med J. 2004;25(3):331-41.
37. Borghi R, Dutra Araujo T, Airoldi Vieira RI, Theodoro de Souza T, Waitzberg DL. ILSI Task Force on enteral nutrition; estimated composition and costs of blenderized diets. Nutr Hosp. 2013;28(6):2033-8.
38. Ambroszkiewicz J, Klemarczyk W, Chelchowska M, Gajewska J, Laskowska-Klita T. Serum homocysteine, folate, vitamin B12 and total antioxidant status in vegetarian children. Adv Med Sci. 2006;51:265-8.
39. Amit M. Vegetarian diets in children and adolescents. Paediatr Child Health. 2010;15(5):303-14.
40. Van Winckel M, Vande Velde S, De Bruyne R, Van Biervliet S. Clinical practice: vegetarian infant and child nutrition. Eur J Pediatr. 2011;170(12):1489-94.
41. Cohen S, Ramirez A, Koch B, Gold B, Millovich V. Weight gain and tolerance in pediatric patients using plant-based enteral formulas. J Ped Gastroenterol Nutr. 2019;69:S281.
42. Viall C, Porcelli K, Teran JC, Varma RN, Steffee WP. A double-blind clinical trial comparing the gastrointestinal side effects of two enteral feeding formulas. J Parenter Enteral Nutr. 1990;14(3):265-9.
43. Campbell SM. An anthology of advances in enteral tube feeding formulations. Nutr Clin Pract. 2006;21(4):411-5.
44. Academy of Nutrition and Dietetics. Evidence-based Nutrition Practice Guideline on Vegetarian Nutrition. 2011.
45. American Academy of Pediatrics Committee on Nutrition. Nutritional Aspects of Vegetarian Diets. In: Kleinmen RD, Greer FR, eds. Pediatric Nutrition. Itasca, IL:American Academy of Pediatrics; 2019. p. 293-311.
46. D'Auria E, Sala M, Lodi F, Radaelli G, Riva E, Giovannini M. Nutritional value of a rice-hydrolysate formula in infants with cows' milk protein allergy: a randomized pilot study. J Int Med Res. 2003;31(3):215-22.
47. Ambroszkiewicz J, Klemarczyk W, Gajewska J, Chełchowska M, Rowicka G, Ołtarzewski M, et al. Serum concentration of adipocytokines in prepubertal vegetarian and omnivorous children. Medicine of Developmental Age. 2011;15(3):326-34.
48. Yen CE, Yen CH, Huang MC, Cheng CH, Huang YC. Dietary intake and nutritional status of vegetarian and omnivorous preschool children and their parents in Taiwan. Nutr Res. 2008;28(7):430-6.
49. Azad C, Jat KR, Kaur J, Guglani V, Palta A, Tiwari A, et al. Vitamin B12 status and neurodevelopmental delay in Indian infants: a hospital-based cross-sectional study. Paediatr Int Child Health. 2020;40(2):78-84.
50. Cofnas N. Is vegetarianism healthy for children? Critical Reviews in food science and nutrition. 2019;59(13):2052-60.
51. Ambroszkiewicz J, Klemarczyk W, Gajewska J, Chelchowska M, Laskowska-Klita T. Serum concentration of biochemical bone turnover markers in vegetarian children. Adv Med Sci. 2007;52:279-82.
52. Ambroszkiewicz J, Klemarczyk W, Gajewska J, Chelchowska M, Franek E, Laskowska-Klita T. The influence of vegan diet on bone mineral density and biochemical bone turnover

markers. Pediatr Endocrinol Diabetes Metab. 2010;16(3):201-4.

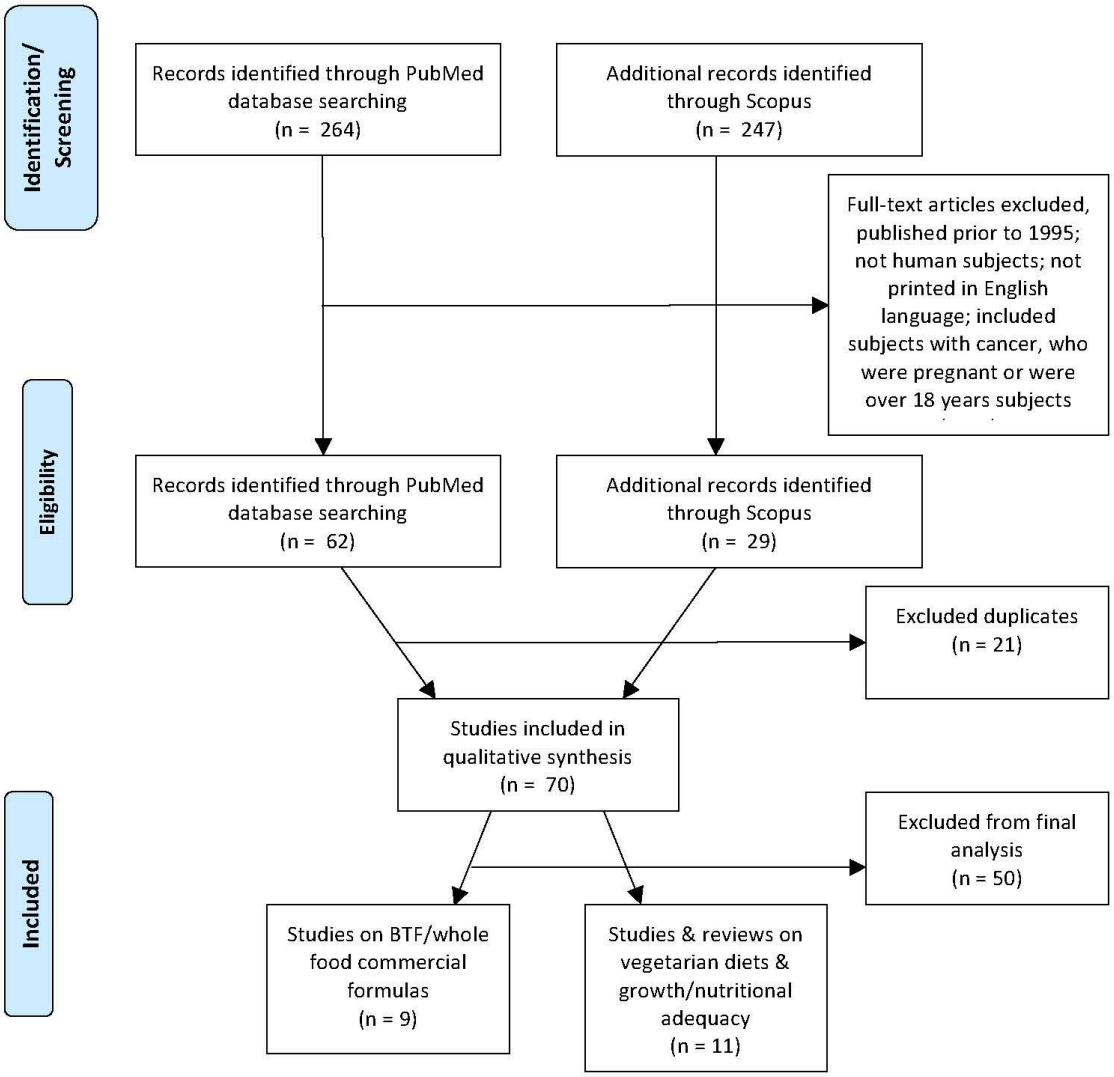
53. Schurmann S, Kersting M, Alexy U. Vegetarian diets in children: a systematic review. Eur J Nutr. 2017;56(5):1797-817.
54. Pawlak R, Bell K. Iron status of vegetarian children: a review of literature. Ann Nutr Metab. 2017;70(2):88-99.
55. Gibson RS. Content and bioavailability of trace elements in vegetarian diets. Am J Clin Nutr. 1994;59(5):1223S-32S.
56. Krajcovicova-Kudlackova M, Simoncic R, Bederova A, Grancicova E, Magalova T. Influence of vegetarian and mixed nutrition on selected haematological and biochemical parameters in children. Nahrung. 1997;41(5):311-4.
57. Institute of Medicine Panel on Micronutrients. Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. Washington (DC): National Academies Press (US).
58. Nathan I, Hackett AF, Kirby S. A longitudinal study of the growth of matched pairs of vegetarian and omnivorous children, aged 7-11 years, in the north-west of England. Eur J Clin Nutr. 1997;51(1):20-5.
59. Messina V, Mangels AR. Considerations in planning vegan diets: children. J Am Diet Assoc. 2001;101(6):661-9.
60. Ambroszkiewicz J, Chełchowska M, Rowicka G, Klemarczyk W, Strucińska M, Gajewska J. Anti-inflammatory and pro-inflammatory adipokine profiles in children on vegetarian and omnivorous diets. Nutrients. 2018;10(9):1241-54.
61. Leung SS, Lee RH, Sung RY, Luo HY, Kam CW, Yuen MP, et al. Growth and nutrition of Chinese vegetarian children in Hong Kong. J Paediatr Child Health. 2001;37(3):247-53.
62. Weder S, Hoffmann M, Becker K, Alexy U, Keller M. Energy, Macronutrient intake, and anthropometrics of vegetarian, vegan, and omnivorous children (1-3 Years) in Germany (VeChi Diet Study). Nutrients. 2019;11(4):832.
63. Hebbelinck M, Clarys P, De Malsche A. Growth, development, and physical fitness of Flemish vegetarian children, adolescents, and young adults. Am J Clin Nutr. 1999;70(3 Suppl):579s-85s.
64. Bhandari N, Bahl R, Taneja S, de Onis M, Bhan MK. Growth performance of affluent Indian children is similar to that in developed countries. Bull World Health Organ. 2002;80(3):189-95.
65. Sabate J, Lindsted KD, Harris RD, Johnston PK. Anthropometric parameters of schoolchildren with different life-styles. Am J Dis Child. 1990;144(10):1159-63.
66. Ambroszkiewicz J, Chelchowska M, Szamotulska K, Rowicka G, Klemarczyk W, Strucinska M, et al. The assessment of bone regulatory pathways, bone turnover, and bone mineral density in vegetarian and omnivorous children. Nutrients. 2018;10(2):183.
67. Movassagh EZ, Baxter-Jones ADG, Kontulainen S, Whiting S, Szafron M, Vatanparast H. Vegetarian-style dietary pattern during adolescence has long-term positive impact on bone from adolescence to young adulthood: a longitudinal study. Nutr J. 2018;17(1):36.

PEER REVIEW

Not commissioned. Externally peer reviewed.

FIGURES

Figure 1. Literature Search and Review Diagram



TABLES

Table 1. Overview of studies assessing outcomes associated with BTF use.

Study	Study Design	Population Size, Characteristics	Type of BTF	Outcome
Quality of Life				
Hron, et al. 2019	Prospective cohort	70 children, ages 1-18 years, who were hospitalized or came through the ED at Boston Children's Hospital receiving BTF vs. SF	Classified in the BTF group if > 50% of their diet was from a BTF. Of the 42 participants receiving BTFs, 40% used homemade BTF with a conventional formula base, 33% used commercial BTFs, and 26% used homemade BTFs	+*
Trollip, et al. 2019	Parental Survey	12 parents of children (ages 1-14 years) on HEN, assessed changes after transition from SF to BTFs	BTF type unspecified, 8 of 12 received SF + BTF	+
Upper GI				
Batsis, et al. 2020	Retrospective	23 children, ages 1-18 years, with G-tube who switched from SF to BTF	Homemade (65%), commercial (17.5%) BTFs or blend of both (17.5%)	+*
Gallagher, et al. 2018	Prospective trial, 6-month feasibility study	20 children, ages 1-16 years, followed at outpatient clinic in Canada were transitioned from SF to BTF over 4 weeks	RDN provided personalized homemade BTF prescription	+*
Hron, et al. 2019	Prospective cohort	70 children, ages 1-18 years, who were hospitalized or came through the ED at Boston Children's Hospital receiving BTF vs. SF	Classified in the BTF group if >50% of their diet was from a BTF. Of the 42 participants receiving BTFs, 40% used homemade BTF with a conventional formula base, 33% used commercial BTFs, and 26% used homemade BTFs	+*
Johnson, et al. 2018	Parental survey	433 parents of children on HEN in an online tube feeding support group, SF (50.5%) and BTF (49.5%)	Homemade BTF (61.8%), commercial BTF (9.2%), blend of homemade and commercial (27.1%), no response (1.9%)	+
McClanahan, et al. 2019	Prospective pilot study	10 children, ages 2-8 years, who transitioned from SF to plant-based, commercial BTF over two months	Commercial, plant-based BTF	+
Pentiuk, et al. 2011	Prospective cohort	33 children post Nissen fundoplication with symptoms of gagging and retching who were receiving gastrostomy feedings	RDN-formulated, pureed foods diet via G-tube	+
Trollip, et al. 2019	Parental Survey	12 parents of children (ages 1-14 years) on HEN, assessed changes after transition from SF to BTFs	BTF type unspecified, 8 of 12 received SF + BTF	+
Lower GI				
Batsis, et al. 2020	Retrospective	23 children, ages 1-18 years, children with G-tube who switched from SF to BTF	Homemade (65%), commercial (17.5%) BTFs or blend of both (17.5%)	-

Hron, et al. 2019	Prospective cohort	70 children, ages 1-18 years, who were hospitalized or came through the ED at Boston Children's Hospital receiving BTF vs. SF	Classified in the BTF group if > 50% of their diet was from a BTF. Of the 42 participants receiving BTFs, 40% used homemade BTF with a conventional formula base, 33% used commercial BTFs, and 26% used homemade BTFs	+*
Johnson, et al. 2018	Parental survey	433 parents of children on HEN in an online tube feeding support group, SF (50.5%) and BTF (49.5%)	Homemade BTF (61.8%), commercial BTF= 9.2%, blend of homemade and commercial (27.1%), no response (1.9%)	+/-
McClanahan, et al. 2019	Prospective pilot study	10 children, ages 2-8 years, who transitioned from SF to plant-based, commercial BTF over two months	Commercial, plant-based BTF	+*
Samela, et al. 2016	Retrospective	10 children (>1 year) who were followed in an intestinal rehab center were weaned from PN and on elemental or semi-elemental SF to BTF	Commercial BTF	+
Trollip, et al. 2019	Parental Survey	12 parents of children (ages 1-14 years) on HEN, assessed changes after transition from SF to BTFs	BTF type unspecified, 8 of 12 received SF + BTF	+
Anthropometric				
Batsis, et al. 2020	Retrospective	23 children, ages 1-18 years, with G-tube who switched from SF to BTF	Homemade (65%), commercial (17.5%) BTFs or blend of both (17.5%)	+*
Epp, et al. 2017	Survey	127 pediatric (avg age 5.4 years) and 91 adult (avg age 51.7 years) patients on HEN	Pediatric population: Homemade (75%), commercial (1%), or a blend of both (24%)	+*
Gallagher, et al. 2018	Prospective trial, 6-month feasibility study	20 children, ages 1-16 years, followed at outpatient clinic in Canada were transitioned from SF to BTF over 4 weeks	RDN provided personalized homemade BTF prescription	+*
Johnson, et al. 2018	Parental survey	433 parents of children on HEN in an online tube feeding support group, SF (50.5%) and BTF (49.5%)	Homemade BTF (61.8%), commercial BTF (9.2%), blend of homemade and commercial (27.1%), no response (1.9%)	+
Pentiuk, et al. 2011	Prospective cohort	33 children post Nissen fundoplication with symptoms of gagging and retching who were receiving gastrostomy feedings	RDN-formulated, pureed foods diet via G-tube	+
Samela, et al. 2016	Retrospective	10 children (>1 year) who were followed in an intestinal rehab center were weaned from PN and on elemental or semi-elemental SF to BTF	Commercial BTF	+
Trollip, et al. 2019	Parental Survey	12 parents of children (ages 1-14 years) on HEN, assessed changes after transition from SF to BTFs	BTF type unspecified, 8 of 12 received SF + BTF	+
Microbiota				
Gallagher, et al. 2018	Prospective trial, 6-month feasibility study	20 children, ages 1-16 years, followed at outpatient clinic in Canada were transitioned from SF to BTF over 4 weeks	RDN provided personalized homemade BTF prescription	+*

McClanahan, et al. 2019	Prospective pilot study	10 children, ages 2-8 years, who transitioned from SF to plant-based, commercial BTF over two months	Commercial, plant-based BTF	+*

+ = Positive outcome for BTF
- = Negative outcome for BTF
* Indicates significant difference ($P < .05$)